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SUBARACHNOID HAEMORRHAGE (SAH) PATIENTS' PAIN MANAGEMENT DURING INTENSIVE CARE PERIOD – A RETROSPECTIVE STUDY

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TIIVISTELMÄ

Ilari Björk & Aukusti Antila: Lukinkalvonalaisen verenvuodon (SAV) sairastaneiden potilaiden kivun hoito tehohoitojakson aikana – retrospektiivinen tutkimus
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Lukinkalvonalaisella verenvuodolla (SAV) on sekä korkea kuolleisuusaste että riski invalidisoiville päätetapahtumille. SAV aiheutuu tyypillisimmin aivovaltimoiden aneurysman puhkeamisesta, aiheuttaen verenvuotoa lukinkalvon alaiseen tilaan. Korkean kuolleisuusasteen sekä vakavien päätetapahtumien lisäksi SAV aiheuttaa potilaille voimakasta ja vaikeasti hoidettavissa olevaa kipua. Potilaat tarvitsevat pääsääntöisesti tehohoitoa, ja tehohoidon aikana kivun monitorointi on haasteellista. Tehohoidon aikana kivunhallinta pohjautuu pitkälti opioidipohjaisiin analgeetteihin. Tutkimuksen tavoitteena on tarkastella SAV:n sairastaneiden potilaiden tehohoidon aikaista kivun hoitoa. Päämääränä on arvioida potilaiden kivun seurantaa sekä kivunhoidon toteutumista.

Tutkimusaineisto koostuu 329:stä Tampereen yliopistollisessa sairaalassa vuosina 2010–2013 tehohoidetusta SAV-potilaasta. Tutkimusasetelma on retrospektiivinen. Tutkimuksessa tarkasteltu hoitojakson pituus oli 14 vuorokautta. Kerätystä aineistosta eriytimme potilaiden subjektiivisen kivun kokemuksen ja muutimme sen tilastollisesti tarkasteltavaan muotoon. Numeerisena asteikkona käytettiin VRS-pisteytystä (verbal rating scale), jossa kliinisen merkitsevyyden raja-arvona toimi yli yhden yksikön muutos pisteissä. Tätä saatua tietoa verrattiin potilaiden saamiin lääkehoitoihin sekä -määriin. Pääasiallisena sekoittavana tekijänä kivun määrityksessä huomioitiin potilaiden tajunnantason aste, jonka arvioimiseen käytettiin Glasgow'n kooma-asteikkoa.

Opioidien käyttö väheni tasaisesti tarkastellun hoitojakson aikana. Samanaikaisesti muiden ei-opioidipohjaisten kipulääkkeiden käyttö lisääntyi vastaavassa suhteessa. Tarkastellun hoitojakson aikana VRS-arvoa ei ollut kirjattu 23,7–48,9 %:lta potilaista, riippuen hoitojakson vaiheesta. Osalla näistä potilaista arvoa ei voitu määrittää matalan tajunnantason vuoksi. Opioidien käytön havaittiin korreloivan kipuarvojen muutosten kanssa. Potilaiden kivunhoidossa käytettävien opioidimäärien päiväkohtainen mediaani vaihteli 12,0–30,2 mg:n välillä oraalista morfiinia hoitojakson aikana. Opioidien käyttö oli pääosin johdonmukaista, annosmäärät vähenivät hoitojakson edetessä.

Kipua koskevat tiedot olivat puutteellisia, ja niitä tulisi kerätä säännöllisemmin analgeettien käytön kohdentamiseksi. Opioidit ovat edelleen ensimmäisen linjan kipulääkkeitä SAV:n kivunhoidossa. Opioidien käyttö korreloi kipuarvojen muutosten kanssa sekä väheni hoitojakson loppua kohden, joten kivun hoidon voidaan katsoa olleen asianmukaista.

Avainsanat: Lukinkalvonalainen verenvuoto, SAV, tehohoito, kivunhoito, opioidi, VRS-pisteytys

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1 INTRODUCTION

Subarachnoid haemorrhage is a devastating disease that carries a high mortality rate and has a severe risk of causing disability, even if the patient goes through normal treatment procedures.(1) The haemorrhage is most often caused by a rupture of an aneurysm in the intracranial subarachnoid space, causing vast bleeding into the subarachnoid space, which induces the rise of the intracranial pressure and the risk of developing a cerebral vasospasm.(2,3) SAH inflicts as many as 800 people every year only in Finland, and therefore is a substantial cause of deaths and disability, especially among the pre-elderly. The occurrence globally is about 1 in every 10.000. Even though the occurrence rate has been slightly decreasing during the last few years, presumably as a result of decreased smoking and more efficient care for high blood pressure, the mortality rate is still as high as 40-45%.(4–6) The single complication with most negative effect on recovery from the SAH is the delayed cerebral ischemia that is connected to 30% of the deaths or poor recovery among the patients with aneurysmal SAH.(7,8) From the 55-65% of people who are not deceased due to SAH, 30% are altered with serious disabilities.(6)

A noticeable factor in the clinical picture of SAH is the substantial amount of pain suffered by the patients. Even though this is well known, there hasn't been much research on the mechanisms of the pain and how it could be better managed during the intensive care period. Due to this matter, there is a significant need for further study on the subject in question. One curiosity is the relationship of experienced pain and pain medication the patients are given during their care period and how it affects the probability of them having delayed cerebral ischemia after their recovery from the SAH. We do not cover this entity in this study, but it is a point of interest requiring further research.

The primary objective of this research is to evaluate the pain management of the SAH patients during their intensive care period. Our purpose is to examine how diligently the pain has been recorded in patients and whether the pain medication that is given to treat the pain is administered according to the amount of pain the patient has reported.

2 MATERIAL AND METHODS

The material used in this research consists of the patient registrations of 329 SAH patients who were treated in the intensive care unit in Tays during the years 2010-2013.

The research method is a retrospective study. Our goal is to extract the patients' verbal descriptions of the experienced pain and transform it into a statistical format. One way to observe this given factor is to examine the amounts and the potency of the pain medication the patients were given. There are also several confounding factors that need to be accounted such as the level of agitation and the state of cognition and consciousness. The statistical scales used to measure these factors are Richard agitation-sedation scale (RASS) and Glasgow coma scale (GCS).

For the recording of pain in the patients we used the Verbal Rating Scale (VRS) which relies on patients' subjective experience of pain. The scale consists of five levels of symptom intensity: 0, 1, 2, 3 and 4 equaling to no pain at all, mild pain, moderate pain, severe pain and intolerable pain respectively.

The modalities of pain treatment included in our study consisted of opioids, NSAIDs, paracetamol, antidepressants (SSRI's and SNRI's) and anticonvulsants (gabapentin and pregabalin). All opioid based analgesics were converted to correspond orally administered morphine.(9) Other forms of analgetic drug therapy were consolidated into same factor "non-opioid based analgesics''.

In addition, we registered patients' temperatures measured during the treatment period, levels of nausea they suffered from, whether they received antimicrobial treatment, their plasma CRP, leukocyte and hemoglobin levels, demand for cardiogenic drugs, demand for sedative drugs and whether they needed invasive respiratory support for over 12 hours during their treatment period.

We chose to examine the patients for the first two weeks of their stay in the intensive care unit to keep the data coherent and easily processable.

3 RESULTS

Out of the patients examined 198 were female and 131 were male. The patients varied by age, youngest being 20 years old and oldest 86 years old. The median age was 56 years. 18 patients suffered from DM, 9 from MCC and 101 from HA.

In our gathered data we found that on the first examined day of treatment 89,7% (n = 329) of patients received some form of analgesic. In contrast on the last examined day the corresponding percentage was 88,1% (n = 42). The most frequently used form of analgesics was opioids as seen in figure 1. Largest subgroups of opioids were intravenous fentanyl and both oral and intravenous oxycodone. The equivalent for most patients were between 10mg and 100mg of oral morphine daily. The need for analgesics stayed constant during the treatment period (FIGURE 1). However, the percentage of opioids as the choice of analgetic slowly decreased in proportion with the duration of the treatment. In the beginning of the treatment period 85,4% (n= 329) of the patients received some form of opioid. The corresponding percentages declined linearly from day 2 on. On day 4 the corresponding percentage is 74,7% (n = 218) and on day 8 59,8% (n = 102). On day 10 the distribution reached 52,1% (n = 71) and stayed mainly constant until the end of our examined treatment period. Also seen is the ascending proportion of non-opioid based analgesics, rising gradually from 4,3% (n = 329) on day 1 to 38,1% (n = 42) on the last examined treatment day.

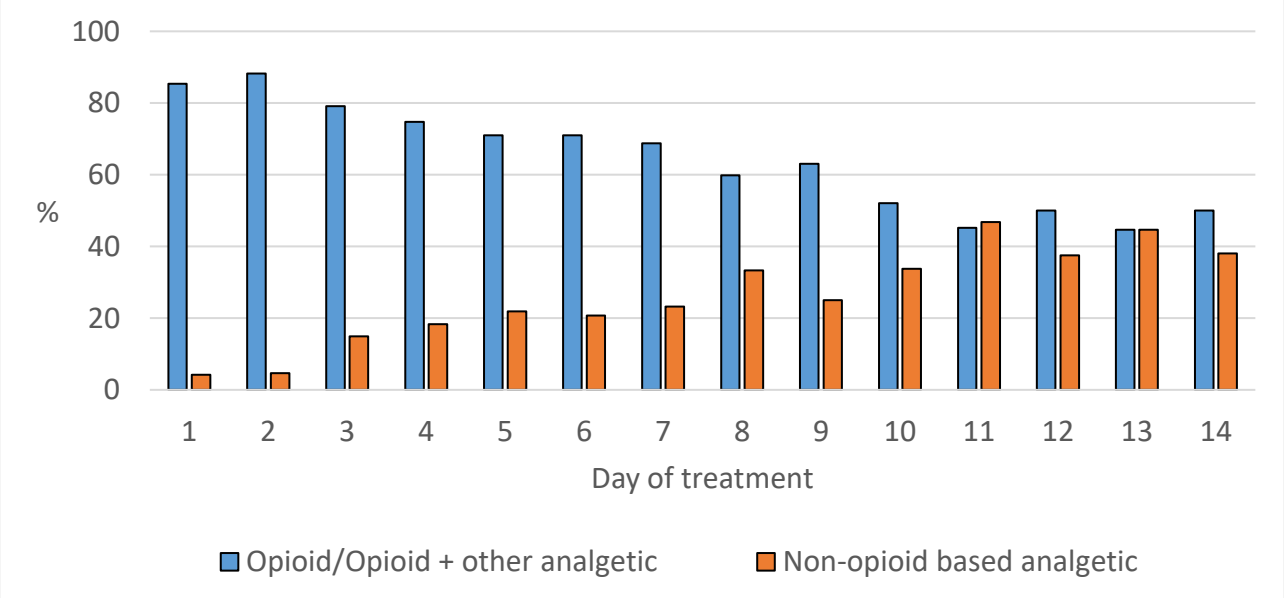

FIGURE 1: the use of analgesics and opioids during the examined treatment period

One of the factors we wanted to examine was the consistency of the measurement and recording of the pain in the patients. Rather than acquiring knowledge of the patients from whom the verbal rating scale (VRS) was measured we wanted to demonstrate the portion of patients whose pain was not recorded. Chart 3 demonstrates that on day one of the examined treatment period the amount of not recorded pain ratings was 35,9% (n = 329). Of these not recorded, 49,1% (n = 118) were patients unable to verbally indicate their experienced pain due to unconsciousness. In this study GCS < 8 was used to represent level of cognition comparable to unconsciousness. On day two of the examined treatment period VRS-score was not recorded from 23,7% (n = 324) of the patients. From there on, the recording of pain not measured increased linearly apart from treatment days 5, 7 and 14 being highest on day 13 (48,9% (n = 47)) of the examined treatment period. The proportion of unconscious patients in relation to those whose pain was not recorded was coherent throughout the examined period.

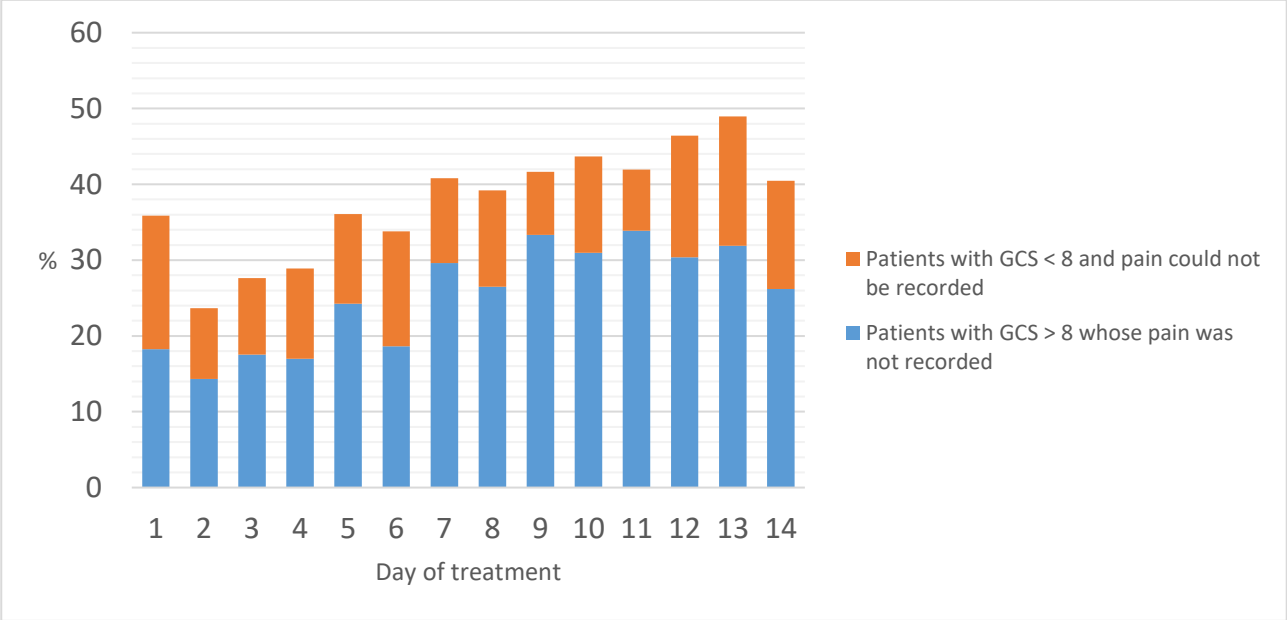

FIGURE 2: Patients with not recorded verbal rating scale and those with Glasgow coma scale score under 8.

The effectiveness of the treatment with opioids can be seen from the figure 3. To assess the adequate use of analgesics in this study the numerical change in VRS being over 1 was seen clinically significant. As seen on figure 3 for each day of the examined treatment period the proportion of patients with non-significant change in their VRS was higher than those of whom had significant change. The ratio between patients with significant and non-significant change increased in

proportion with the duration of the examined treatment period. To a certain extent a correlation was found in patients subjective pain ratings depending on whether the patients were given opioids. However, there is also a big subdivision of non-responders and in addition to that many of those treated with opioids seemed to have a low pain rating to begin with. This evokes a question whether the pain medication was used for the treatment of pain in these patients or for some other indication.

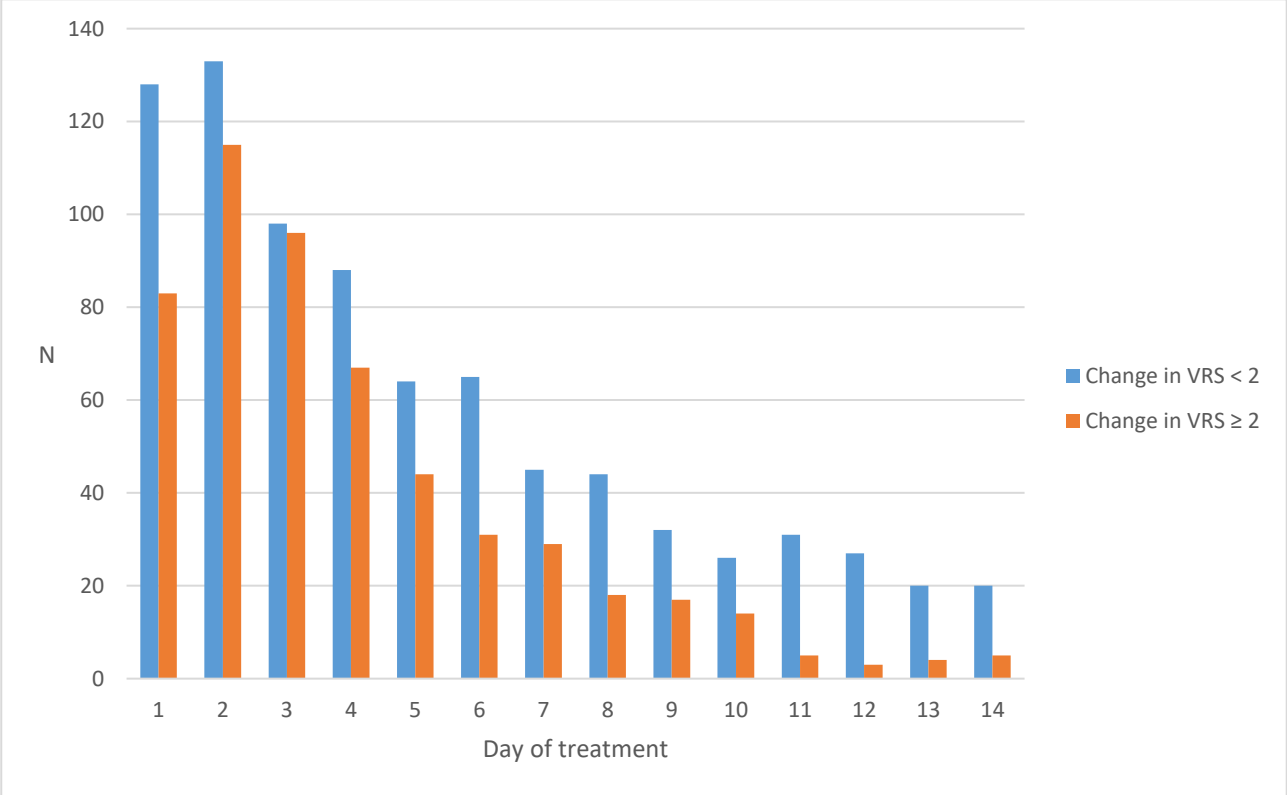

FIGURE 3: Change of verbal rating scale score during the examined treatment period with the threshold value being 2.

In addition to the volume of opioid use we also studied the amounts of opioids those patients receiving opioid therapy were given. As seen on figure 4 the opioid use was constant throughout the examined treatment period varying from the lowest median amount of 12,0 mg of oral morphine on day 14 to the highest of 30,2 mg on day two. The quantity of opioid use was mainly adequate excluding singular outliers receiving over 10-fold times the daily median amount. The daily maximum doses rose up to 700 mg on said outliers.

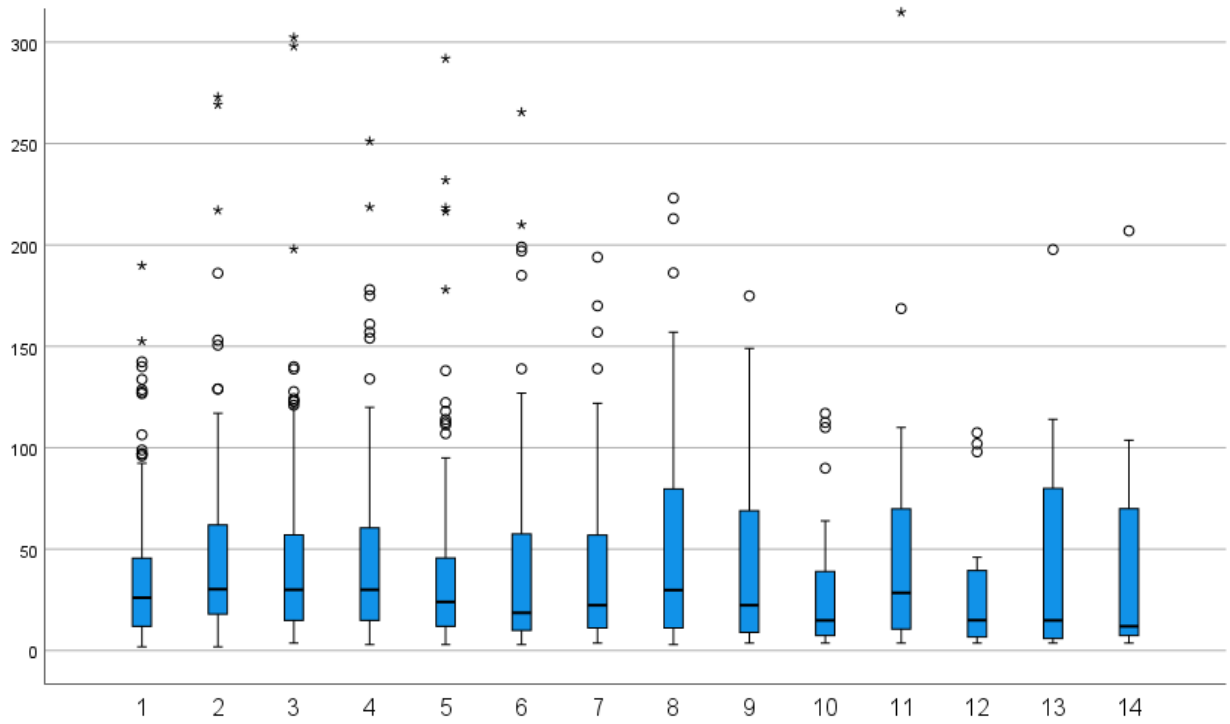

FIGURE 4: Opioid quantity during the examined treatment period.

4 DISCUSSION

The results demonstrate comparatively high usage of opioids and other pain treatment modalities. In relation to the medicine use, the lowering of pain in the patients correlates relatively well to the pain treatment. However, a significant percentage of patients treated with opioids didn't see a sizeable change in their pain ratings. This might partially be due to the ratings being low or at most moderate in the first measuring timepoint. One other factor that could lead to these kinds of findings is that opioids lack the potency to relieve SAH induced pain as the pain mechanism is not fully understood at this point of time, although it is thought that the headache is primarily due to the chemical irritation of the blood on the brain meninges, combined with the pressure effects and possible other more minor factors. (10)

Regarding the findings based on figure 3 a question is brought up whether the opioids were administered off-label for some other indication, such as agitation, restlessness, or incoherence in addition to actual pain treatment. Figure 4, which demonstrates opioid quantity during the examined treatment period, shows outliers receiving 10-fold times the daily median opioid amount. On further inspection these patients were receiving fentanyl as an infusion and the indication was most probably sedation rather than pain management.

Further investigation is needed to come into conclusion about whether other pain management modalities possess potential to overcome opioids as the main method of pain management. The adverse effects of opioids are well known and are prone to cause problems later in the treatment, especially if the duration of treatment is extended.(11) Part of the adversities come into play after patients have been discharged from intensive care unit to primary health care for rehabilitation. Significant use also makes the assessment of patients' cognitional recovery more difficult both during their intensive care period and later in their rehabilitation.(12)

A question regularly thought of during our research is whether the appropriate management of pain influences the prognosis of the disease. When assessing the success of pain treatment, most emphasis is naturally placed on the factor of relieving humane suffering. This is undisputedly the core purpose of pain treatment. However, when assessing the patient's recovery as a whole, most value is generally

placed on the level of functioning the patient recovers to. Reflecting on this, it is also important to assess the effect the appropriate treatment of pain has on this factor.

More research is also needed to conclude whether there could be more accurate ways of measuring pain rather than just their verbal estimation. The ways for more systematic reporting of pain are something that should be looked into in the intensive care units around the world. CPOT has been shown to be somewhat competitive, but it is still seen only as a moderate tool for measuring pain and more research needs to be done to conclude its effectiveness in SAH subgroup.(13)

One point of interest is the verbal rating scale's reliability as the used parameter of the measured pain. Patients' general feeling of discomfort may lead to higher pain rating and therefore other factors such as level of sedation and anti-anxiety and anti-nausea medicines might have a remarkable effect on the ratings. A lot of confounding factors affect the patient's subjective sensation of pain. There is no certainty to the matter how did the other medication such as sedatives and anti-hypertensives affect the patients experience of pain. SAH patients are prone to relatively high levels of sedation and use of sedative substances that alters the patients' level of consciousness and the ability to report pain. Most robust reasons for prolonged sedation duration are elevated ICP and status epilepticus.(14)

Questions which rose on basis of our data include the absence of regularly seizing ASA and anticoagulants in patients that had recently suffered a bleed. ASA's anti-inflammatory mechanisms have been suspected to contradict the inflammatory process of smoking and therefore even lower the risk for spontaneous SAH, but further research is needed. It is also subject to consideration whether low dose ASA as an anti-inflammatory drug may possess analgesic potential decreasing the amount of pain suffered from these inflammatory processes. (15–17)

We recorded several confounding factors such as antimicrobial treatment, blood samples including CRP, leukocytes and hemoglobin and different types of medications. This data was not used in this study, but it is something to take into consideration when doing further studies.

In summary, the data demonstrates that the trend of opioid usage and the amounts used was generally coherent and stayed constant during the whole period of examination. There is a significant lack of research focusing on opioid usage as an analgesic for SAH. Due to this limitation, it is hard to find reference values on this given subject. In the studies we examined, the amounts of opioids used were notably higher than in our study. In a cross-sectional study conducted in the US by Klavansky *et al.*

the mean daily morphine equivalent dosage during their hospitalization was 18.74 mg intravenously. Similar findings were in a cohort study conducted in The John Hopkins University in US by Morad *et al.* the findings were similar to the ones by Klavansky *et al.* with the mean intravenous morphine equivalent dose was 15.7 mg per day. Reason for the differences in results of our study and the reference studies are left unanswered. One potential factor could be the lack of global consensus on the treatment of SAH associated pain. In Finland the use of opioids is also relatively conservative, especially compared to the US which is amongst the nations with the highest consumption of opioids in the world. (17–19)

Our findings concerning the changes in VRS being relational with the usage of analgesics and the progression during the treatment period were logical and implied a satisfactory response to the treatment. Similar kind of findings were reported in a South Korean study by Hong *et al.* which used NRS (numerous rating scale) as a measuring factor. They reported that 89.3% of patients reported improvement in headache upon discharge. Improvement was defined as decline of the NRS score from moderate or severe (4-6 and 7-10 respectively) to a score of 3 or under. *(*20)

4.1 LIMITATIONS:

In this study the reliability of the pain data gathered on the first day of treatment is suspect to error due to differences in the admission times of different patients. If the time frame was shorter, it is possible that there has been some prioritizing in treatment procedures which then leads to lower percentages for pain recording.

Retrospective register study has some limitations due to its nature. Most notable limitation being the absent pain recordings. Other limitations include the lack of patients' opinions regarding their pain treatment, having no possibility for follow-up of patients after their discharge from intensive care unit and the exclusion of accounting non-medical treatment of pain.

4.2 CONCLUSIONS:

1) Data regarding pain is deficient, pain data should be gathered regularly to aim the analgesics use.
2) Opioids are still the mainstream analgesic despite alternative medications and known side-effects.

3) The use of opioids correlated with changes in pain values and decreased towards the end of the treatment period, so the use can be considered to have been appropriate.

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