



Analgesic and psychoactive medications and the risk of falls in relation to delirium in single-bed rooms compared to multiple-bed rooms in geriatric inpatients

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Abstract

Background Previously, we demonstrated a substantial reduction of delirium incidence among geriatric patients after relocating from old hospital buildings with multiple-bed rooms to a new hospital with single-bed rooms.

Aims To investigate whether (1) the reduced incidence of delirium in single-bed rooms was associated with a simultaneous change in medication use, (2) the relocation had affected the incidence of falls, (3) the use of analgesics and psychoactive medications was associated with the risk of delirium and falls.

Methods We included 461 admissions to the old wards and 553 admissions to the new wards. Delirium was assessed by the Confusion Assessment Method. Data on drug use and falls during hospitalization were extracted from medical records.

Results There was no difference in drug use between the wards. In the new wards, patients who had experienced delirium had a much higher risk of falls than patients without delirium, while in the old wards this contrast was small. The risk of delirium was increased among patients who received antipsychotic drugs and anti-dementia drugs. Patients who received these drugs had an insignificantly increased risk of falls.

Conclusion Medication of analgesics and psychoactive drugs was similar in the old and new wards. In single-bed rooms, but not in multiple-bed rooms there was a much higher risk of falls among inpatients that developed delirium than among other patients. Patients who had used antipsychotics and anti-dementia drugs during hospitalization had increased risk of developing delirium and an insignificantly higher risk of falls.

Keywords Geriatric · Hospital design · Single-bed room · Delirium · Falls · Analgesic · Psychoactive drug

Background

Geriatric patients are characterized by multimorbidity, cognitive impairment, physical disability, malnutrition, falls, polypharmacy and iatrogenic complications, and dependence of personal assistance. All these characteristics increase the risk of delirium. Delirium is a common mental syndrome in hospitalized older patients with serious adverse implications and high health care costs [1]. During hospitalization, the risk of delirium varies from 11 to 42% in general medical

inpatients, and for frail older inpatients prevalences up to 60% are described [1, 2]. In our geriatric department, the risk of delirium was reduced from 29% to 16% in connection with relocation from an old hospital with multi-bed rooms to a new hospital with single-bed rooms [3].

Delirium is characterized by acute inception of fluctuations in the mental state. The clinical characteristics of delirium include decreased ability to maintain attention. The patients are incoherent in thinking and speech, and they have reduced memory and a changing level of consciousness, ranging from awake to lethargic, drowsy or inaccessible [1]. Delirium often causes restlessness, gait disturbance, dizziness, blurred vision, muscle weakness, and an increased risk of falls [4–6].

For many years, medications that affect the central nervous system have been suspected of increasing the risk of delirium and falls in older patients. Only few clinical studies have investigated the associations between use of opioids

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and the risk of delirium or falls. Severe pain and especially undertreated pain after surgery has been associated with postoperative delirium [7]. However, Sieber et al. found no association between postoperative delirium and use of opioids neither for cognitively impaired nor cognitively intact patients [8]. On the other hand, a Canadian study found that recent opioid use was associated with an increased risk of falls in older patients [9].

Few drugs for mental illness have been associated with the development of delirium. In a case–control study, Marcantonio et al. found that postoperative delirium was associated with both long-acting and short-acting benzodiazepines [10], and the use of benzodiazepines among older patients has been shown to increase the risk of falls [11]. Evidence for an association between delirium or falls and drugs for mental illness or dementia in older patients is inconsistent or not existing.

Objectives

The aim of this paper is to investigate whether the reduced incidence of delirium in the new hospital with single-bed rooms was associated with a simultaneous change in the use of medications. We also examine whether the relocation of the department to a modern hospital had affected the incidence of falls, both among delirious and non-delirious patients. Finally, we examine whether the use of analgesics and psychoactive medications is associated with the risk of delirium and falls among patients in a geriatric department.

Patients and methods

Study design and patients

The study design is described in detail in a previous paper [3]. Patients 75 years or older admitted for neurological, medical or surgical reasons to the Geriatric Department at Aarhus University Hospital were included. Patients were consecutively admitted to the old hospital with multiple-bed rooms (old wards) between 15 September 2016 and 19 March 2017 and to the new hospital with single-bed rooms (new wards) from 20 March to 19 December 2017. Patients could be included once to the same ward. Exclusion criteria were terminal illness, somnolence and inability to communicate in Danish.

The old wards consisted of two geriatric wards located at different addresses. There were five three-bed rooms, eleven two-bed rooms and two single-bed rooms with 13 shared bathrooms. The new wards are located on two different floors in the same building. In total, there are 32 single-bed rooms with own bathroom. Visiting time is unrestricted, and

a relative can stay overnight in the room, which was very inconvenient in the old wards.

Measurements of delirium

At admission to the Geriatric ward, all enrolled patients were tested for delirium by the geriatric staff using a Danish translation of the Confusion Assessment Method (CAM) [12]. Until discharge, the patients were assessed every morning and evening with CAM or, in a few cases, examined by a physician to diagnose delirium. Delirium at admission was defined as a positive CAM score at the first screening. New cases of delirium during hospital stay were defined as occurring after the first screening. For patients who experienced delirium during hospital stay, the observation time was divided in two periods, before and after start of delirium. Other patients were classified as not being exposed to delirium throughout their hospital stay. All measurements of CAM were registered in the electronic patient record and consequently copied to the research database by one of the authors (SB). If CAM was missing in a patient record, the relevant staff member was contacted for completion.

As preparation for the present study, the geriatric staff members, comprising nurses, nurse assistants, occupational therapists and physiotherapists fulfilled a course on delirium and treatment in geriatric patients, including the Danish version of the training manual and coding guide for CAM followed by a test [12]. This preparation took place before inclusion of the first patients, and new staff tended the same course before performing CAM screenings. For more detailed information, see the previous paper [3].

Exposure to analgesics and psychoactive drugs

From the medical records for the current hospitalization, the following ATC-codes were extracted: natural opium alkaloids (opioids) (N02AA), other opioids (N02AX), antipsychotics (N05A), anxiolytics (N05B), hypnotics and sedatives (N05C), antidepressants (N06A), and anti-dementia drugs (N06D) [13]. We recorded the date of first use of a medication and analysed the dosage of risperidone, as risperidone is used for treatment of delirium in our department. We did not include dosage or treatment duration for other medications in the analysis.

Measurements of falls

Falls were defined as fall from chair or bed or from standing or walking, and as episodes where the staff found the patient lying or sitting on the floor. It is mandatory to report falls as accidental events to The Danish Patient Safety Authority Register and in the electronic patient

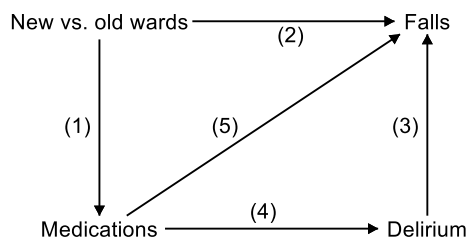


Fig. 1 Associations analysed in this paper

records. Time from admission to the first fall was recorded. The number of falls per patient was not included in the analysis.

Measurements of comorbidity

Charlson Comorbidity Index was calculated from all diagnoses recorded in the patient journal for the current admission. A diagnosis of dementia was identified at the current or prior admissions or from information from the patient’s general practitioner [14]. For more detailed information, see the previous paper [3].

Statistics

An overview of the main analyses in this paper is shown in Fig. 1. We used Cox regression to compare [1] the use of medications and [2] the risk of falls in the old and the new wards, [3] the risk of falls in relation to delirium, and [4] the risk of delirium and [5] the risk of falls in relation to medications. The analyses were validated by a test of the proportional hazards assumption. Some patients were admitted both once to the old and once to the new wards, and to adjust for this clustering, we used robust variance estimates. Any *p* value less than 0.05 was considered statistically significant. Statistical analyses were performed with Stata software, version 15.1. (StataCorp LLC, College Station, Texas, USA).

Ethics

The study was part of a quality development project with no intervention. It was evaluated by the Central Denmark Region Ethical Committee, which considered it to be non-experimental, and a formal approval was therefore not required. The study protocol was approved by the

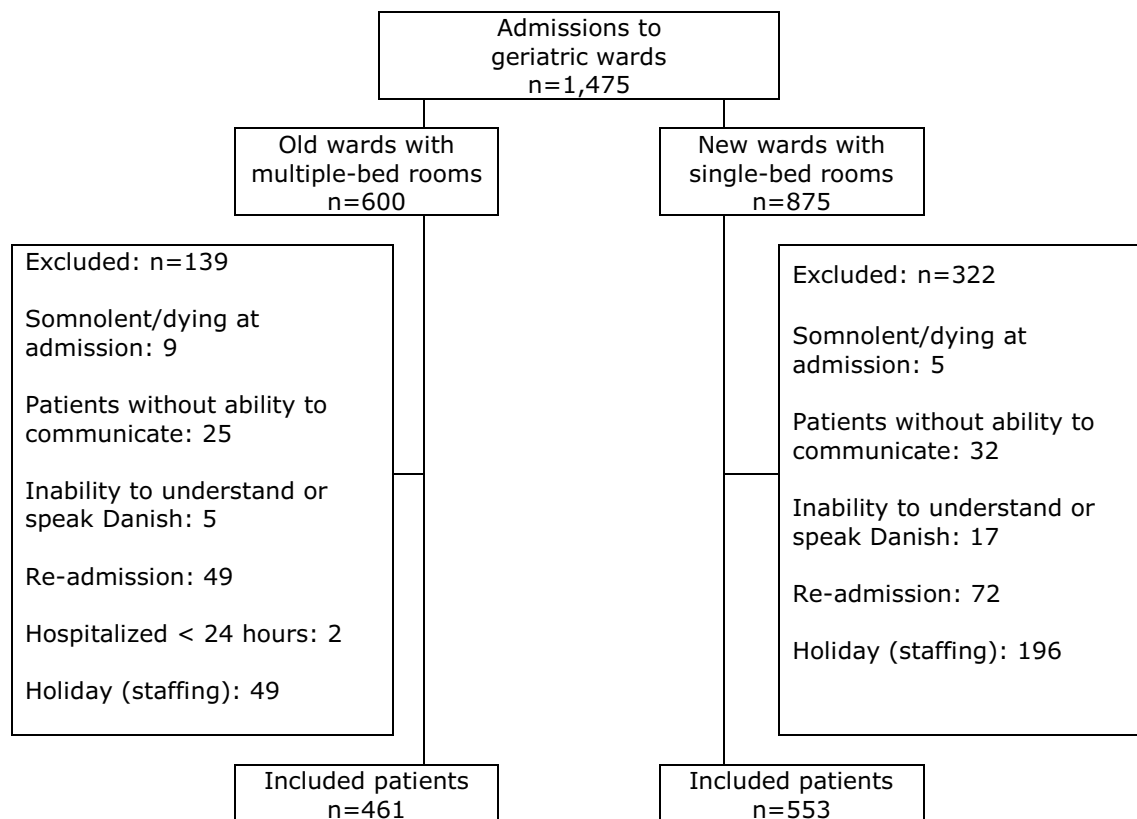


Fig. 2 Flow chart

Danish Data Protection Agency, case no. 1-16-02-254-16. Data were stored according to good research practice. The study was registered at ClinicalTrials.gov (Identifier NCT03199768).

Results

The study includes 1014 admissions among 964 different patients; 50 patients were admitted both to the old and the new ward. See flowchart in Fig. 2.

Baseline patient characteristics were well balanced (Table 1). For 105 admissions (10%), delirium was present at the first screening, with no significant difference between the wards. The most common causes of admission were infection (31%) and fractures (20%) with no statistically significant difference between the wards.

Table 2 shows the use of analgesic and psychoactive drugs. There were no significant differences in use between the two wards. Table 2, fourth column shows hazard ratios (HR) for delirium in relation to prior medications. Patients who received other opioids had a decreased risk to develop

delirium, while patients who received antipsychotic or anti-dementia drugs had an increased risk.

In total 36 patients received risperidone; five in the old wards and seven in the new wards received risperidone by admission and for reasons other than delirium. In the old wards the median dose was 1.5 mg (IQR 0.5 mg–5 mg) and in the new wards 2.5 mg (IQR 1 mg–5.5 mg), $p=0.40$.

In the old wards, 26 (6%) patients and in the new wards 23 (4%) had experienced one or more falls during hospitalization; the difference was insignificant, HR = 0.81 (95% CI 0.46–1.42). Patients with delirium had an increased risk of falls, HR = 4.68 (95% CI 2.58–8.46, $p < 0.001$). There was however, a significant interaction between ward type and delirium on the risk of falls, $p=0.008$. As illustrated in Fig. 3, the contrast in the incidence of falls between patients with and without delirium was modest in the old wards, while there was a strong contrast in the new wards.

Table 3 shows the risk of falls among patients receiving a particular drug; there was an insignificantly increased risk of falls among users of antipsychotics and anti-dementia drugs.

Table 1 Baseline characteristics of 1014 geriatric admissions

Baseline characteristics	Old wards with multiple-bed rooms. Number (%) or median (IQR ^a)	New wards with single-bed rooms. Number (%) or median (IQR ^a)	<i>p</i> value
<i>N</i>	461	553	
Age	87 (82–91)	86 (81–90)	0.05
Sex (male)	169 (36%)	233 (42%)	0.08
Length of stay, days	7 (5–9)	6 (5–8)	0.35
Living arrangements			
Own home	434 (94%)	504 (91%)	0.14
Nursing homes	27 (6%)	49 (9%)	
Medical history			
Prior diagnosis of dementia	40 (9%)	49 (9%)	0.92
Falls	50 (11%)	51 (9%)	0.40
Delirium at admission	48 (10%)	57 (10%)	0.96
Charlson comorbidity index			
0 (none)	151 (33%)	183 (33%)	0.83
1–2 (low)	216 (47%)	274 (49%)	
3–5 (moderate)	81 (18%)	81 (15%)	
6–12 (severe)	13 (3%)	15 (3%)	
Physical ability (MBI) ^b			
Minor (100–80)	54 (12%)	76 (14%)	0.61
Slight (79–50)	143 (31%)	161 (29%)	
Moderate (49–26)	134 (29%)	162 (30%)	
Severe (25–0)	127 (28%)	150 (27%)	
BMI ^c	23.7 (21–27.1)	23.8 (20.9–26.9)	0.87

^aInterquartile range, i.e. 25% and 75% percentiles

^bModified Barthel Index-100 (Missing: 7)

^cMissing: 33

Table 2 Use of analgesic, benzodiazepines and antipsychotic drugs during hospitalization

	Old wards with multiple-bed rooms. No. patients (%)	New wards with single-bed rooms. No. patients (%)	Medications new vs. old wards Hazard ratio (95% CI)	Hazard ratio (95% CI) for delirium after medication vs. no prior medication
Natural opium alkaloids (opioids) (N02AA)	228 (49)	268 (48)	1.01 (0.86–1.18)	1.13 (0.88–1.46)
Other opioids (N02AX)	27(6)	39 (7)	1.16 (0.61–2.19)	0.45 (0.21–0.97) ^a
Antipsychotic (N05A)	25 (5)	35 (6)	1.28 (0.68–2.38)	2.54 (1.61–4.01) ^a
Anxiolytics (N05B)	21 (5)	21 (4)	0.81 (0.41–1.62)	0.94 (0.42–2.11)
Hypnotics and sedatives (N05C)	94 (20)	106 (19)	0.97 (0.69–1.35)	1.03 (0.69–1.53)
Antidepressants (N06A)	135 (29)	155 (28)	0.89 (0.72–1.11)	1.13 (0.86–1.48)
Anti-dementia drugs (N06D)	19 (4)	20 (4)	0.69 (0.35–1.37)	2.45 (1.46–4.11) ^a

^aStatistically significant difference

Discussion

Analgesics

There was no difference in the use of opioids between the old and the new wards. In addition, there was no association between use of natural or other opioids and falls. Also, the use of natural opioids was not associated with delirium.

For patients who used other opioids such as tramadol, the incidence of delirium was decreased. This is in contrast to previous studies. In a frail geriatric population, Laurila et al. found tramadol and codeine as precipitating factors for delirium [15]. This was confirmed by Brouquet et al. who found tramadol administration to be a strong risk factor for delirium in older postoperative patients [16]. We believe that the contrast between these studies and our more recent study is due to an increased awareness of tramadol being a risk factor for delirium, leading to restrictive use in high-risk patients. Only 66 (7%) inpatients used tramadol, and we do not know whether they used it prior to the admission.

Psychoactive drugs

There was no difference in the use of psychoactive drugs in the old wards and the new wards. Holdensen et al. investigated the use of haloperidol, expressed as defined daily dosages, during a change from multiple-bed rooms to single-bed rooms. They found that the use decreased by 50%. We used risperidone rather than haloperidol in the treatment of delirium, and we found neither difference in the number treated nor the dosage between the old and the new wards. Holdensen et al. did not record the occurrence of delirium [17].

The incidence of delirium was increased among patients who had used antipsychotics prior the first episode of delirium. It probably reflects that the underlying psychiatric disorder both increases the risk of delirium and affects the

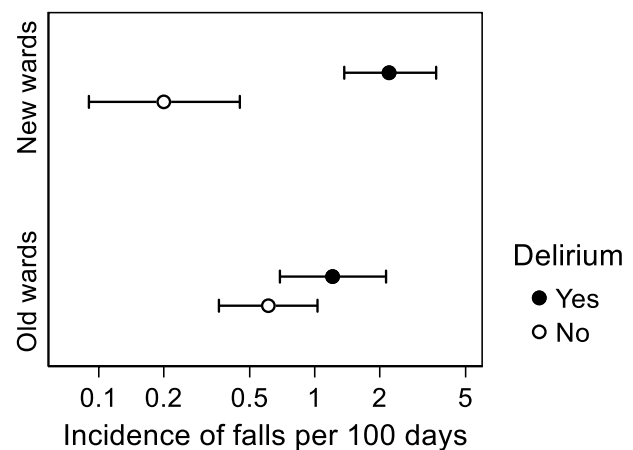


Fig. 3 Incidence of falls in relation to ward type and delirium

use of antipsychotics, but a direct effect of the medication on the risk of delirium cannot be excluded in the present observational study.

For patients who used anti-dementia drugs, the risk of delirium was increased. It is well-known that the risk of delirium is associated with dementia [1, 18, 19], and it might explain the observed association between anti-dementia drugs and delirium. However, the present observational study cannot determine whether there is a direct positive or negative effect of anti-dementia drugs on the risk of delirium.

Use of psychoactive drugs was not associated to the risk of falls among older hospitalized patients.

Falls

We found an apparently strong and significant effect of delirium on the incidence of falls in the new wards, while

Table 3 Use of analgesic and psychoactive medications and the risk of falls

Medication exposure	Number exposed	Patients with falls (%)	Risk ratio (95% CI) ^a
Regardless of exposure	1014	49 (5)	–
Natural opium alkaloids (opioids) (N02AA)	496	23 (5)	0.92 (0.53–1.60)
Other opioids (N02AX)	66	2 (3)	0.61 (0.15–2.46)
Antipsychotics (N05A)	60	6 (10)	2.22 (0.98–5.00)
Anxiolytics (N05B)	42	1 (2)	0.48 (0.07–3.41)
Hypnotics and sedatives (N05C)	200	10 (5)	1.04 (0.53–2.05)
Antidepressants (N06A)	290	19 (7)	1.58 (0.90–2.76)
Anti-dementia drugs (N06D)	39	4 (10)	2.22 (0.84–5.87)

^aThe risk ratio compares users and non-users of the medication

the effect of delirium in the old wards seemed modest. We hesitate to attempt explaining this finding. As previously demonstrated, the risk of delirium was reduced among patients in the new wards [3]. This could point to a high degree of frailty among patients who developed delirium despite the favourable environment in the new wards, while the remaining patients could benefit from the environment in new wards. We can not exclude that absence of supervision in single-bed rooms could be a risk factor for fall in delirious patients.

The higher risk of falls among delirious inpatients is in agreement with results by Mazur et al. and by Stenvall et al. [5, 6].

Strengths and limitations of the study

It is a strength of the study that we were able to calculate a precise assessment of whether the medication was given before or after delirium started.

The main limitation of the study is the lack of knowledge about the patients' use of medications prior to admission. Therefore, it is unknown whether there was a different use of opioids and psychoactive drugs prior to admission in the two wards and for patients with and without delirium. Furthermore, it was only possible to compare the dosages of risperidone in the analysis, and there might have been differences in the dosage of other medications between the two wards.

We believe that there were very few, if any, missed falls. In the geriatric wards, the staff is focusing on fall registration, and typically, geriatric patients can hardly get up from the floor without assistance after a fall.

Moving the geriatric department to modern hospital involved several changes, and the study does not allow deciding with certainty which changes were responsible for the reduced incidence of delirium. The staff completed the same course before using CAM, and the clinical guidelines for delirium did not change. The staff turnover did not change in relation to the relocation of the department and there was no change in uptake area. We believe that the

change to single-bed rooms had a major impact, but other changes like more space, quiet rooms, better access to daylight, better working conditions for the staff, or improved indoor climate might also play a role.

Conclusion

New wards with single bedrooms were not associated with change in medication use for analgesic and psychoactive drugs compared to old wards with multiple-bed rooms. Patients who had used antipsychotics and anti-dementia drugs during hospitalization had increased risk of developing delirium, but this was most likely due to the condition both leading to medication and the risk of delirium. The present study cannot determine whether there is a direct positive or negative effect of the use of these drugs and the risk of delirium.

Finally, in the new wards with single-bed rooms there was a higher risk of falls among inpatients that developed delirium compared to inpatients without delirium. We did not find the same contrast in the old wards with multiple-bed rooms. Antipsychotics and anti-dementia drug may increase the risk of falls.

Compliance with ethical standards

The cost of data collection, analysis, and preparation of the manuscript was covered by the Department of Geriatrics, Aarhus University Hospital.

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Research involving Human Participants It was a quality development project with no intervention, the study was exempted from notification to the Central Denmark Region Ethical Committee (Inquiry number 200/2017). The study protocol was approved by the Danish Data Protection Agency, case no. 1-16-02-254-16. The study was registered at ClinicalTrials.gov (Identifier NCT03199768).

Informed consent Not needed according to Ethical Committee.

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