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Gender-specific differences in nursing staff's administration patterns of 'pro re nata' medication: A prospective observational study

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Abstract

Background: Pro re nata'(PRN) medications are important parts of the management of critically ill patients. PRN medications are predominantly administered by nurses, and indications, frequencies and doses of PRN might be influenced by experience, attitude, and empathy. Since it is advocated that empathy has a gender-specific pattern, we compared the PRN prescription model in female and male nurses.

Methods: On the Operative ICU of a University Hospital, 1000 shifts (each 500 male and female nurses) were prospectively analyzed regarding PRN medications via a Patient Data Monitoring System. The data collection included characteristics of nurses and patients, and the severity of illness. PRN medication was analysed qualitatively and quantitatively.

Results: Female nurses tended to perform less night shifts and more morning shifts compared to male, and female nurses cared significantly more frequent for female patients. In a major area of patient comfort, sedative and analgesic PRN medication, we found no statistically different gender-specific patterns. For constipation, the average amount of polyethylene glycol was significantly higher ($p = 0.018$) when prescribed by female nurses (189.3 ± 62.7 ml) compared to male nurses (170.9 ± 60.5 ml). For cardiovascular instability, male nurses applied significantly higher ($p = 0.011$) cumulative doses of norepinephrine (5.4 ± 5.8 mg vs. 4.1 ± 4.3 mg).

Conclusions: In this first assessment of potential gender differences in the administration of PRN medications, we found only minor differences in two categories of medication (gastrointestinal and cardiovascular support), with no difference in the major element of suffering (pain and anxiety).

Introduction

The majority of ICU patients suffer from illness-/diagnostics-/therapy-/medication-related side effects, such as agitation, pain, nausea/vomiting or hypotension [1-4]. The handling of these symptoms has a considerable influence on the patient's outcome [1,2,4-8]. Antiemetics, cathartic medicine, analgosedatives and blood pressure medication are often prescribed on a 'pro re nata' (PRN) or 'as needed' basis. In these cases, time points of prescription, doses and frequencies are not scheduled but can be individually adjusted to the patient's needs [9-11]. The 'need for medication' may be expressed verbally or nonverbally by the patient, depending on his/her condition, or identified via assessments by the caretaker [12,13]. Furthermore, the prescription pattern of PRN might be influenced by beliefs, attitudes, perceived norms, perceived behavioral control, intentions, and experience. Bedside nurses can be in charge for the administration of PRN medication, given that they are present at the bedside more often than the physicians [11,14,15]. This has been shown to lead to a quicker treatment, in case that PRN medication can be given autonomously by the nurses within the limits of the physician's prescription [11,15-18]. Consequently, this comes along with a high grade of freedom of action and responsibility for the care staff [10,12,19].

For the specific concept of PRN medication empathy, defined as the ability to share the internal state of another person [20-22] might be a fundamental requirement. It is assumed to be one of the main motivators for prosocial behaviour [21-23]. Since previous studies offer evidence for a correlation between gender and empathy [22,24,25], we performed an observational study to test the hypothesis that female nurses give higher amounts of PRN medication due to stronger affective empathy and emotional responsivity to other's pain and discomfort compared to men. The knowledge about gender-specific trends in the treatment of ICU patients may help to sensitize staff for personal medication patterns aimed at improving the quality of PRN medication therapy.

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Methods

Study design and population

We conducted a prospective observatory single centre study from January 2016 to Mai 2016 in the Regensburg University Hospital, Germany, a tertiary care referral hospital. The patient collective refers to an adult Operative ICU ward consisting of 26 beds. In total, 1000 shifts were analysed regarding the administered PRN medication, contrasting two groups: Shifts done by female (in the following: f-shift) and those done by male (in the following m-shift) nurses, 500 each. Data about nursing staff, patients and medication were obtained from a patient data monitoring system (PDMS, MetaVision, Imd-soft, Amsterdam, The Netherlands). Shifts were chosen randomly and would be excluded if they met one or more of the following criteria: patient in need of palliative care, indication for reanimation of the patient, specific nurse-patient-mating had already been included in study, shift data included implausible or missing values. The nurses were not informed about the study. All data were processed anonymously. The study was approved both by the Regensburg University Ethics Committee (approval no 15-104-0354) and the worker's council.

The data collection included three shifts (morning [6:15 – 14:30]; medium [14:00 – 21:30]; and night [21:00-6:45]), the nurse's sex and age, and characteristics of the patient (sex, age, number of days already spent at the ICU, status of isolation due to multiresistant specimen, and the severity of illness as per the SAPS II (Simplified Acute Physiology Score) and TISS 10 (Therapeutic Intervention Scoring System). No pain assessment scales were used. PRN medication was analysed qualitatively (drugs administered) and quantitatively (cumulative overall dose per shift).

The selection of relevant PRN medication included the most frequently prescribed PRN medication:

I. cathartic medicine: polyethylene glycol, sodium picosulfate, lactulose, castor oil, enema

II. blood pressure medication/catecholamines: syringe pump/ bolus: norepinephrine

III. analgesics: syringe pump: sufentanil, bolus: hydromorphon, metamizol, oxycodon/naloxon, generic oxygesic inj., piritramide

IV. sedatives: syringe pump: clonidin, propofol, bolus: midazolam, lorazepam

Statistical analysis

Data were pooled and analysed using SPSS (IBM SPSS statistics 23.0). We examined baseline demographics and staff/patient's characteristics using mean ± standard deviation for continuous variables and percentage for categorical variables. All drug doses were checked for plausibility. Descriptive analyses were calculated for all variables.

For the comparison of shifts done by male nurses with those done by female nurses, we used the chi-squared test (for categorical variables) and the *t* test or Mann–Whitney *U* test (for continuous variables) as appropriate. All tests of significance were two-tailed, and *p* value of 0.05 was considered significant.

Results

Of 1000 shifts analysed for this study, 42 had to be excluded for implausible or missing values. In total, the adjusted data set consisted of 958 shifts, of which 476 were done by male and 482 by female nurses. The mean time spent in the ICU was not different in the cohorts of male and female shifts.

Nurses' and patients' collectives

Nurses ranged in age from 20 to 64 years, the average age was slightly higher for male nurses (Table 1). Women tended to do more morning shifts compared to their male colleagues who accordingly had a higher proportion of middle and night shifts. Interestingly, the proportion of male patients was significantly higher in m-shifts than in f-shifts. The mean age of patients did not differ significantly for m- and f-shifts, as well as the number of days the patient had already spent at the ICU, the ratio of isolated patients and the severity of illness according to the SAPS II and TISS 10.

Comparison of medication in M-/F-shifts

The analyses of general and gender-specific medication trends are made separately for four PRN medication subgroups (cathartic medicine/laxatives, blood pressure modulating drugs, analgesics, and sedatives).

Cathartic medicine

In total, the administration of one or more laxative could be registered in 684 of 958 shifts (71.4%). Predominantly, they were given during morning (58.9%) and middle shifts (37.1%); administration during night shifts was rare (Table 2). In case of laxative use, the predominating substances being given were polyethylene glycol, sodium picosulfate and lactulose. The application of enema and castor oil was rather unusual (5.1% and 4.5%). Interestingly, a significant difference occurred regarding the application of polyethylene glycol, the most frequently used laxative; it was almost 20 ml higher in median in f-shifts than in m-shifts (p = 0,018). Other cathartic treatments did not differ significantly between male and female nurses.

Blood-pressure modulation/vasoactive agents

Catecholamines were given in 450 cases, meaning 47.0% of the shifts analysed, continously applied through the day. The predominant application mode was the continuous administration of Norepinephrine via syringe pump (SP, Table 3). Only 8.2% of the patients got bolus applications (B) of either Norepinephrine (5.1%), Dobutamine (2.4%) or Epinephrine (0.7%).

The total amount of Norepinephrine given per shift (Figure 1) was significantly higher in m-shifts (5.3 mg) compared to f-shifts (4.1 mg, p= 0.011). Bolus applications did not show significant differences or could not be analysed for the little quantity of values collected.

Analgesics

In 768 of 958 shifts analgesics were administered (Table 4), mostly during middle shifts, followed by morning shifts and night shifts. In total, 1114 single administrations were recorded, of which metamizole was the most common (30.1%), hydromorphone and sufentanyl ranged around 20%. Oxycodone/naloxone was administered in approximately 12% of the cases. Substances used rather rarely were generic oxygesic inject and piritramide. Female Nurses were slightly more probable to give analgesics than male nurses (m:78.2%, f: 82.2%, p= 0.124). No statistically significant gender-specific differences were observed concerning the quantity of medication administered.

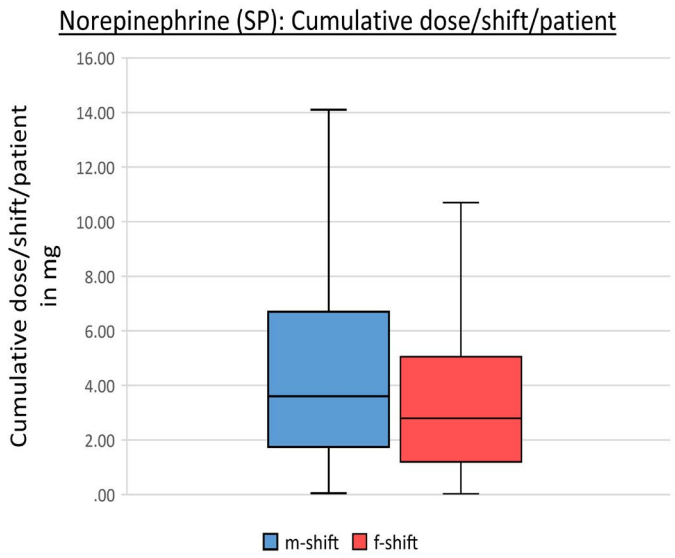

Figure 1. Characteristics of administration of norepinephrine.

Table 1. Characteristic data of nurses and patients involved in the study.

	Male nurses	Female nurses	p-value (Sig. two-tailed) 1: T-/Mann-Whitney-U-Test 2: Chi-Square-Test
Nurse collective			
Quantity of shifts (%)	476 (49.7)	482 (50.3)	
Mean age (min/max)	32.4 ± 8.5 (21/64)	30.3 ± 9.4 (20/57)	.000 (1)
Shift			
Morning (%) Middle (%) Night (%)	148 (31.1) 183 (38.4) 145 (30.5)	182 (37.8) 171 (35.5) 129 (26.8)	.090 (2)
Patient Collective			
Male (%) Female (%)	320 (67.2) 156 (32.8)	275 (57.1) 207 (42.9)	0.003 (2)
Mean Age	64.6 ± 14.0	63.1 ± 14.5	0.091 (1)
Days already spent at the ICU	8.7 ± 11.0	8.3 ± 9.0	0.538 (1)
SAPS II	20.0 ± 11.0	20.0 ± 10.3	0.925 (1)
TISS 10	9.7 ±7.1	10.3 ± 7.3	0.194 (1)
Isolated patient (%)	111 (23.3)	131 (27.2)	0.181 (2)

Sedatives

Sedatives were administered in about 30% of the shifts (330 of 958) steadily during the day (Table 5). The most frequently used substance in over 60% of the cases was propofole, applicated by syringe pump. The use of clonidine, lorazepam and midazolam ranged between 12.3 and 11.8% each. Male and female nurses didn't differ significantly in the administration patterns of sedative medication, meaning frequency, quantity or quality.

Discussion

'As needed` medication in intensive care, regarding the application of cathartic medicine, acute blood pressure regulation, analgesics, or sedatives is predominantly given by nurses. The demand for 'pro re nata' (PRN) drugs is assessed by the nurse staff, and time points of description, doses and frequencies are influenced by the grade of qualification, experience, and attitude of the nurses. Since empathy was found to be an important motivator for compassionate and prosocial behavior we were interested in gender-specific differences among the prescription of PRN medication in an intensive care setting. To our knowledge no study including such a study design was performed yet.

The main results of our study are: 1) Female nurses tended to perform less night shifts and more morning shifts compared to male, and female nurses cared significantly more frequent for female patients. 2) In general, PRN were mostly prescribed in the middle shift, except for cathartic drugs in the morning. 3) No difference in the major element of suffering (pain and anxiety) managed by the nurses with PRN medications was found. 4) Only minor differences in two categories of medication were observed: The average amount of gastrointestinal medication (polyethylene glycol) was significantly higher (p = 0.018) when prescribed by female nurses compared to

Table 2. Characteristics of administration of cathartic medicine.

≥ 1 administration/shift (%)	Total: 418 (100.0) Morning: 246 (59.0) Middle: 155 (37.1) Night: 17 (4.0)		
Number of single administrations - total - by substances (%)	684 (100.0) Movicol: 295 (43.1) Laxoberal: 211 (30.9) Lactulose: 115 (16.8) Enema: 32 (5.1) Castor Oil: 31 (4.5)		
	Male Nurses	**Female Nurses**	p-value (Sig. two-tailed) 1: T-/Mann-Whitney-U-Test 2: Chi-Square-Test
Share of shifts with ≥ 1 administration in %	42.6	44.6	.558 (2)
Mean cumulative dose administered/Pat/Shift (administration preconditioned)			
Polyethylene glycol (ml)	170.9 ± 60.5	189.3 ± 62.7	**0.018** (1)
Sodium picosulfate (ml)	1.0 ± 0.1	1.1 ± 0.8	0.884 (1)
Lactulose (ml)	16.0 ± 7.6	15.7 ±7.2	0.825 (1)
Castor Oil (ml)	16.2 ± 15.0	18.1 ± 11.9	0.709 (1)
Enema (no of applications)	1.7 ± 0.9	1.2 ± 0.5	0.058 (1)

Table 3. Characteristics of administration of blood pressure medication/catecholamines (SP = syringe pump, B = bolus)

≥ 1 administration/shift (%)	Total: 418 (100) Morning: 140 (33.5) Middle: 149 (35.6) Night: 129 (30.9)		
Number of single administrations - total - by substances (%)	450 (100.0) Norepinephrine (SP): 413 (91.8) Norepinephrine (B): 23 (5.1) Dobutamine (B): 11 (2.4) Epinephrine (B): 3 (0.7)		
	Male Nurses	**Female Nurses**	p-value (Sig. two-tailed) 1: T-/Mann-Whitney-U-Test 2: Chi-Square-Test
Share of shifts with ≥ 1 administration in %	42.2	44.8	.474
Mean cumulative dose administered/Pat/Shift (administration preconditioned)			
Norepinephrine-SP. (mg)	5.4 ± 5.8	4.1 ± 4.3	**0.011 (1)**
Noradrenalin-Bol. (mg)	0.03 ± 0.03	0.03 ± 0.03	0.571 (1)

Table 4. Characteristics of administration of analgesics (SP = syringe pump, B = Bolus)

≥ 1 administration/shift (%)	Total: 768 (100.0) Morning: 284 (37.0) Middle: 294 (38.3) Night: 190 (24.7)		
Number of single administrations - total - by substances (%)	1114 (100.0) Metamizole (B): 335 (30.1) Hydromorphone (B): 257 (23.1) Sufentanyl (SP): 255 (22.9) Oxycodone/naloxone: 132 (11.9) Generic oxygesic inj.: 78 (7.0) Piritramide (B): 57 (5.1)		
	Male Nurses	**Female Nurses**	p-value (Sig. two-tailed) 1: T-/Mann-Whitney-U-Test 2: Chi-Square-Test
Share of shifts with ≥ 1 administration in %	78.2	82.2	0.124 (2)
Mean cumulative dose administered/Pat/Shift (administration preconditioned)			
Metamizole (B) (g)	1.3 ± 0.8	1.4 ± 0.8	0.285 (1)
Hydromorphone (mg)	5.0 ± 3.0	4.9 ± 2.6	0.644 (1)
Sufentanyl (SP) (microgr.)	318.4 ± 191.7	329.2 ± 211.6	0.671 (1)
Oxycodon/Naloxon (mg)	13.6 ± 6.1	14.8 ± 8.2	0.366 (1)
Oxygesic inj. (mg)	5.7 ± 4.4	6.3 ± 4.5	0.579 (1)
Piritramide (mg)	6.7 ± 4.2	5.9 ± 3.8	0.438 (1)

Table 5. Characteristics of administration of sedative agents (SP = syringe pump, B = bolus)

≥ 1 administration/shift (%)	Total: 330 (100.0) Mornig: 104 (31.5) Middle: 120 (36.4) Night: 106 (32.1)		
Number of single administrations - total - by substances (%)	390 (100.0) Propofol (SP): 246 (63.1) Clonidine (SP): 50 (12.8) Lorazepam: 48 (12.3) Midazolam (B): 46 (11.8)		
	Male Nurses	**Female Nurses**	p-value (Sig. two-tailed) 1: T-/Mann-Whitney-U-Test 2: Chi-Square-Test
Share of shifts with ≥ 1 administration in %	52.1	47.9	0.278 (2)
Mean cumulative dose administered/Pat/Shift (administration preconditioned)			
Propofole 2% (SP) (mg)	892.8 ± 571.4	967.6 ± 610.9	0.323 (1)
Clonidine (SP) (mg)	0.3 ± 0.3	0.3 ± 0.2	0.367 (1)
Lorazepam (mg)	1.2 ± 0.8	0.9 ± 0.2	0.159 (1)
Midazolam (B) (mg)	8.3 ± 8.7	7.8 ± 5.8	0.857 (1)

male nurses. 5) On the other hand, male nurses applied significantly higher ($p = 0.011$) cumulative doses of norepinephrine compared to the female staff.

PRN medication use has increased as standard practice in acute patient care, but in recent studies a poor documentation of prescription and administration of these drugs was found [11,18]. In our study, we used a patient data management system, which has been established a longer time ago and all the intensive care staff were strictly committed to document every medication. In a recent study from Korea [9], the differences in prescription and perception of PRN was assessed at five hospitals, and administration errors were observed, since nurses were more likely to conduct PRN administration by their own decision, which often did not meet the physicians order. On our ICU, a 'freedom' of prescribing and administering PRN within a range of demands or distress was arranged between doctors and nurses, and no errors or conflicts were reported. Sun and coworkers [19] examined the difference between the prescribed and actually administered doses of analgesic and sedative drugs in ICU patients, and they found that 'narcotics' and benzodiazepines were most often used. Interestingly, the amount of nurse-administered midazolam was below the maximum ordered by physicians, while more opioid infusions (fentanyl) were given than the ordered dose. The authors conclude that physicians tended to write fairly nonspecific orders that were used by the nurses as very broad guidelines.

Empathy as a capacity to resonate with another person's emotional state through shared affect (pain, sadness, distress, pleasure, satisfaction) involves both emotional and affective components. Women typically are seen to have superior trait empathy compared with men [25]. But some critiques on such a possible 'stereotypic' gender image were expressed by other researchers and they argued that the recent studies on gender-specific differences in empathy fault largely due to cultural expectations about gender roles. On the other hand, some authors found evidence that sex differences in empathy have biological, phylogenetic and ontogenetic roots, and are not merely cultural byproducts [22]. In our study, we noted that the prescription pattern of sedatives and analgesics was not different between female and male nurses. Obviously, the advocated *sex differences in empathy for pain* [25] could not be reconfirmed with our data. A possible explanation could be that gender-related differences in empathy for pain, which were stated in 'older studies', might be highly driven by the assessment instruments. In an actual study with a modern empathy-for-pain paradigm assessed in 10.000 healthy volunteers, no major gender-effects were found [26]. The authors conclude that 'traditional' instruments or self-reports may induce biases or gender-role stereotypes.

Nevertheless, in our study female nurses administered more cathartic medicine and male nurses applied more blood-pressure stabilizing agents (norepinephrine). There is a lack of data describing the evidence-based use of laxatives in critically ill patients. In a small observational study [27] in 50 patients performed at a medical intensive care unit, in 25 patients no bowel movement was observed via ultrasound examination during the first 96 hours of admission. In these patients, the administration of a stimulant laxative was associated with bowel movement. Guidelines for the use of laxatives in ICUs are not available. In a field study [28], the use of norepinephrine in intensive care was studied. Nurses and physicians of 14 ICUs in France were given questionnaires on the way they use norepinephrine, and as a result it was observed that only 25% of the prescribers indicated the systematic use of hemodynamic monitoring.

Our study has strengths and limitations. The strength is the prospective and strict recording and assessment of PRN medication based on a patient data management system used by nurses who are 'educated' for an easy and consequent documentation of each measure they perform. The main limitation is the concept as a single center study, but we believe that the analysis of a large number of shifts allows a justified conclusion.

In summary, gender-specific differences in the prescription of 'pro re nata' medication were only found in the administration of minor

important PRN drugs (laxative agents and blood pressure stabilizing drugs), while no difference in the major element of suffering (pain and anxiety) managed by the nurses was observed.

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