Prescribing preferences in rapid tranquilisation: a survey in Belgian psychiatrists and emergency physicians

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Abstract

Background: The pharmacotherapeutic management of agitation is a common clinical challenge. Pharmacotherapy is frequently used, the use of published guidelines is not known. The purpose of this study was twofold; to describe the prescribing patterns of psychiatrists and emergency physicians and to evaluate to which extent guidelines are used.

Methods: A cross-sectional survey in the Dutch-speaking part of Belgium is carried out in 39 psychiatric hospitals, 11 psychiatric wards of a general hospital and 61 emergency departments. All physicians are asked for demographic information, their prescribing preferences, their use of guidelines and the type of monitoring (effectiveness, safety). For the basic demographic data and prescription preferences descriptive statistics are given. For comparing prescribing preferences of the drug between groups Chi square tests (or in case of low numbers Fisher’s exact test) were performed. McNemar test for binomial proportions for matched-pair data was performed to see if the prescription preferences of the participants differ between secluded and non-secluded patients.

Results: 550 psychiatrist and emergency physicians were invited. The overall response rate was 20% (n = 108). The number 1 preferred medication classes were antipsychotics (59.3%) and benzodiazepines (40.7%). In non-secluded patients, olanzapine (22.2%), lorazepam (21.3%) and clozapine (19.4%) were most frequently picked as number 1 choice drug. In secluded patients, clozapine (21.3%), olanzapine (21.3%) and droperidol (14.8%) were the three most frequently chosen number 1 preferred drugs. Between-group comparisons show that emergency physicians prefer benzodiazepines significantly more than psychiatrists do. Zuclopenthixol and olanzapine show a particular profile in both groups of physicians. Polypharmacy is more frequently used in secluded patients. Published guidelines and safety or outcome monitoring are rarely used.

Conclusions: Our results show that prescription practice in Flanders (Belgium) in acute agitation shows a complex relationship with published guidelines. Prescription preferences differ accordingly to medical specialty. These findings should be taken into account in future research.

Keywords: Agitation, Rapid tranquilisation, Emergency psychiatry, Guidelines

Background

Agitated behaviour during a hospital admission is a frequently encountered problem. It is estimated that yearly 1.7 million hospital admissions occur due to agitation [1, 2]. About 10% of the patients admitted to the emergency department are at risk of developing agitation symptoms [3]. Agitation is seen in conjunction with different psychiatric and non-psychiatric medical conditions [4–6].

Although motor restlessness, increased responsiveness to stimuli, irritability, inappropriate and usually purposeless verbal and motor activity are reported as the major hallmarks of the syndrome, there is no consensus regarding the symptoms that constitute agitation. Little...
is known about its course over time and which level of
agitation should lead to pharmacological treatment [7, 8].
This ambiguities all hamper the development of general-
izable clinical guidelines [9]. Although good clinical trials
have been conducted to investigate the effectiveness and
the safety of drugs prescribed in agitated behaviour [10–
12], results should be interpreted cautiously in clinical
practice, given that these trials have better internal than
ecological validity [13–15]. Consequently, prescribing
preferences may not always be based on evidence based
guidelines, although the use of drugs in this indication is
widely spread [1, 2, 9, 15].

In order to map prescribing habits of physicians in
acute agitation, a series of studies—surveying physicians’
preferences—was conducted between 1999 and 2004
[10, 12, 16–20]. While they all differ in methodological
design, do not compare between psychiatrists and emer-
gency physicians, and are all service-specific or region
specific, a few trends can be found in these reports.
Firstly, antipsychotics (olanzapine, haloperidol and dro-
peridol) and benzodiazepines (diazepam, lorazepam) are
the preferred drugs of choice. Secondly, there is no real
preference for peroral or intramuscular administration.
Thirdly, there is a reported trend in favour of using com-
binations of drugs.

The present study was conducted with a twofold
objective. We firstly aimed to describe the prescribing
preferences and their between group differences of psy-
chiatrists and emergency physicians in Belgium in the
management of acute agitation and secondly we evalu-
ated to which extend prescribing preferences were in
accordance with published treatment guidelines.

Methods
A cross-sectional online survey was carried between
the July 2012 and September 2012 in 39 psychiatric hos-
pitals, 11 psychiatric wards of a general hospital and
61 emergency departments. 281 psychiatrists and 267
emergency physicians received an invitation to respond
to the survey. Participating psychiatrists and emergency
physicians were asked to give demographic and profes-
sional information, describe their prescribing habits in
the treatment of acute agitation, their use of evidence
based guidelines and the type of monitoring (effectiv-
ness, safety) they provide for their patients. Agitation was
defined in the survey as a clinical condition with acute
onset of psychomotor and emotional excitement. The fol-
lowing parameters were collected: age, gender, medical
specialty, medical setting, number of patients with agita-
tion admitted in 1 month, use of rating scales, preference
of drug prescribed, use of drugs in combinations, effect
of seclusion on prescription preference, use of guidelines
and modalities of monitoring of efficacy as well as patient

First, it was evaluated which medication classes and
specific drugs were preferred and if preferences changed
in the case the patient needed seclusion. Second, we
looked for differences in prescribing habits depending on
the medical specialty.

For the basic demographic data and prescription pref-
ferences descriptive statistics are given. For each drug,
two Chi square tests (or in case of low numbers Fisher’s
exact test) were performed, one comparing prescribing
preferences of the drug between psychiatrists and emer-
gency physicians and another one comparing prescribing
preferences between age groups. Mc Nemar test for bino-
rial proportions for matched-pair data was performed
to see if the prescription preferences of the participants
differ between secluded and non-secluded patients.

IBM SPSS Statistics version 20.0 was used for statistical
analyses.

Results
Response rate and respondents characteristics
110 psychiatrists and emergency physicians responded
to the online survey, yielding a response rate of 20%.
Two of them were removed from further analysis as they
reported treating 0 patients per month for agitation.
From the 108 respondents, 69 (63.9%) were male and 39
(36.1%) were female. Psychiatrist accounted for 65.7%,
emergency physicians for 34.3%. Sixty-seven respond-
ents were between the ages of 25 and 45 years of age, 41
respondents were older than 45 years. Physicians worked
in different settings; 42 (38.9%) in a psychiatric hospital,
25 (23.1%) in a psychiatric ward of a general hospital
and 41 (38.0%) in an emergency service. A caseload
for agitation between 1 and 10 patients per month was
reported by 69 (63.9%) of the participants, 23 (21.3%) had
a monthly caseload between 11 and 20 and 16 (14.8%)
reported a caseload higher than 20 patients.

Preferences in medication prescriptions
General preferences for a medication class in acute agitation
Respondents were asked to point out which of five medi-
cation classes (antipsychotics, antidepressants, benzo-
diazepines, mood stabilizers and antihistaminics) they
favoured in the treatment of acute agitation. They had to
give the classes a number from 1 to 5 with 1 being the
most preferred class, 2 the second preferred class,... All
respondents chose either antipsychotics (59.3%) or ben-
zodiazepines (40.7%) as their number 1 preferred medi-
cation. As a number 2 medication class benzodiazepines
were most preferred (54.6%). The number 3 medication
class that was most popular are the mood stabilizers
(37.4%), number 4 are the antidepressants (38.3%) and number 5 are the antihistaminics (44.9%).

Rankings for all medication classes are shown in Table 1.

**Prescribing preferences in non-secluded patients**

All participants were given a list of 80 drugs and were asked to select their 3 most used drugs when considering all patients in need for a treatment of agitation and rank these according to preference, rank 1 being their first choice drug. All rankings are listed in Table 2. Olanzapine (22.2%), lorazepam (21.3%) and clotiapine (19.4%) were the three most popular first choice drugs. Most frequently ranked second were lorazepam (21.3%), olanzapine (17.6%) and droperidol (12.0%). As a third choice, clotiapine (13%), lorazepam (11.1%) and olanzapine (11.1%) were reported most frequently. Although zuclopenthixol does not appear but in third choice (2.8%), the long acting formula of this drug is reported more frequently (1.9% as first choice; 2.8% as second choice; 8.3% as third choice).

Of the participants 107 answered the question on the use of monotherapy versus combinations, 21.5% of them reported to use only monotherapy whilst 67.3% use a combination of drugs in a step-up regimen and 11.2% a combination of drugs from the start of the treatment.

**Prescribing preferences in secluded patients**

We also investigated what the prescription preferences were when patients were considered that are in need of a seclusion room as a non-pharmacological approach to agitation. 62% of the participants adapt their drug choice (38% of participants reported not to change their prescription preferences in this type of patients).

Participants were asked to give their top 3 drugs for secluded patients from the same list of 80 drugs (rankings are shown in Table 2). Clotiapine (21.3%), olanzapine (21.3%) and droperidol (14.8%) were reported the most frequently as first choice. Most frequently ranked second were lorazepam (22.2%), diazepam (13.9%) and clotiapine (12.0%). Most mentioned number 3 drugs were lorazepam (13.0%), haloperidol (12.0%), clotiapine (10.2%), droperidol (10.2%) and zuclopenthixol long formula (10.2%). Again, zuclopenthixol does not appear but as third choice (3.7%). However, the long acting formula of this drug is reported more frequently than in the non-secluded group of patients (6.5; 3.7; 10.2%).

For the treatment of secluded patients 107 respondents answered the question on the use of monotherapy versus combinations. 15.9% reported to use only monotherapy whilst 59.8% use a combination of drugs in a step-up regimen and 24.3% a combination of drugs from the start of the treatment.

**Differences in medication preferences for psychiatrists and emergency physicians**

For non-secluded patients all participants ranked either atypical antipsychotics or benzodiazepines as their first choice used drugs, we use a Chi square test to see if there is a difference between first choice use among psychiatrists and emergency physicians. Only 19 of the 71 psychiatrists (26.8%) classified benzodiazepines as their preferred product whereas 25 of the 37 emergency physicians (67.6%) did so. This difference in preference was significant (Chi square test \( p < 0.001 \)).

No differences in preference between psychiatrists and emergency physicians was found for conventional antipsychotics (clozapine, haloperidol, zuclopenthixol en zuclopenthixol long acting) (psychiatrists; 27 (38%) and emergency physicians; 10 (27%); Chi square test \( p = 0.253 \)) but a significant difference was found for atypical antipsychotics (aripiprazole, olanzapine, risperidone, quetiapine) (psychiatrists; 27 (38%) and emergency physicians; 7 (19.8%); Chi square test \( p = 0.042 \)).

The analysis of differences in preference for specific drugs in non-secluded patients are listed in Table 3. The first three columns use for the considered drug the criterium: did the participant rank this as number 1 drug? The last 3 columns use as criterium: did the participant put this drug in its top 3? The number of positive answers to this criterium together with the percentages of either professional group are given. A Fisher’s exact test was performed for each drug. Psychiatrists place quetiapine and zuclopenthixol (long acting formula) significantly more than emergency physicians in their top 3 of used drugs. In contrast, midazolam, diazepam and haloperidol are significantly more in the top 3 of emergency physicians.

In secluded patients, psychiatrists \( [n = 12 (16.9%)] \) classified a benzodiazepine as their preferred product whereas this was significantly higher in the emergency physicians group \( [n = 18 (48.6%)] \); Chi square test \( p < 0.001 \).

A significant difference was found in preference between psychiatrists and emergency physicians for

| Table 1 Overview of number 1–5 preferred medication classes |
|-----------------------------|----------------|----------------|----------------|----------------|
| AP | BZD | AD | MS | AH |
| 59.3 | 40.7 | 0 | 0 | 0 |
| 40.7 | 54.6 | 1.9 | 1.9 | 0.9 |
| 0 | 1.9 | 31.8 | 37.4 | 29.0 |
| 0 | 1.9 | 38.3 | 34.6 | 25.2 |
| 0 | 0.9 | 28.0 | 26.2 | 44.9 |

*AP* antipsychotics, *BZD* benzodiazepines, *AD* antidepressants, *MS* mood stabilizers, *AH* antihistaminics.
conventional antipsychotics (psychiatrists; 39 (54.9%) and emergency physicians; 11 (29.7%); Chi square test $p = 0.013$) but this was not the case for atypical antipsychotics (psychiatrists; 20 (28.2%) and emergency physicians; 7 (18.9%); Chi square test $p = 0.292$). The analysis of differences in preference for specific drugs in secluded patients are listed in Table 4 analogously to Table 3. Psychiatrists place olanzapine, zuclopenthixol (long acting formula) and quetiapine significantly more in their top 3 than emergency physicians. In contrast, diazepam, haloperidol and midazolam, are placed in the top 3 significantly more amongst emergency physicians.

### Differences in medication preferences for age-groups

The total sample of respondents was splitted into a group of prescribers that was younger than 45 years of age ($n = 67$, 62%) and a group older than 45 years of age ($n = 41$, 38%). When non-secluded patients were to be considered by the respondents, it was found that older physicians ($n = 6$) tended to prefer droperidol as their number 1 choice drug over their younger peers ($n = 1$, Fisher’s exact $p = 0.012$) whereas a trend was observed for lorazepam as number 1 choice drug in favour of the younger physicians ($n = 18$) versus older peers ($n = 5$, $p = 0.091$). Further, no significant age effect on prescription preferences was found for all other drugs. When secluded patients were to be considered by the respondents, no significant effect for doctor’s age was observed except for zuclopenthixol long formula in the top 3 of favourite drugs which was preferred by older peers ($n = 15$) versus younger physicians ($n = 7$, $p = 0.002$). The same trend as seen for lorazepam as number 1

### Table 2 Prescribing preferences in non-secluded and secluded patients

| Drug               | Non-secluded patients | Secluded patients |
|--------------------|-----------------------|-------------------|
|                    | Rank 1                | Rank 2            | Rank 3            | Rank 1 | Rank 2 | Rank 3 |
|                    | Frequency %           | Frequency %       | Frequency %       | Frequency % | Frequency % | Frequency % |
| Alprazolam         | 2 1.9                 | 5 4.6             | 1 0.9             | 1 0.9   | 4 3.7   |
| Alprazolam (LA)    | 1 0.9                 |                   |                   | 1 0.9   | 1 0.9   |
| Amisulpride        | 3 2.8                 | 1 0.9             | 3 2.8             | 4 3.7   | 1 0.9   |
| Aripiprazole       | 1 0.9                 |                   |                   | 1 0.9   | 1 0.9   |
| Bromazepam         | 4 3.7                 | 5 4.6             | 7 6.5             | 4 3.7   | 6 5.6   | 7 6.5   |
| Clonazepam         | 21 19.4               | 8 7.4             | 14 13             | 23 21.3 | 13 12.0 | 11 10.2 |
| Clozapine          | 5 4.6                 | 10 9.3            | 5 4.6             | 6 5.6   | 15 13.9 | 5 4.6   |
| Diazepam           | 7 6.5                 | 13 12             | 8 7.4             | 16 14.8 | 12 11.1 | 11 10.2 |
| Droperidol         | 2 1.9                 | 2 1.9             | 2 1.9             | 2 1.9   | 3 2.8   | 2 1.9   |
| Escitalopram       | 23 21.3               | 23 21.3           | 12 11.1           | 14 13   | 24 22.2 | 14 13   |
| Haloperidol        | 24 22.2               | 19 17.6           | 12 11.1           | 23 21.3 | 12 11.1 | 8 7.4   |
| Lamotrigine        | 1 0.9                 |                   |                   | 1 0.9   | 1 0.9   |
| Lorazepam          | 5 4.6                 | 12 11.1           | 5 4.6             | 3 2.8   | 6 5.6   | 3 2.8   |
| Midazolam          | 2 1.9                 | 2 1.9             | 3 2.8             | 1 0.9   | 2 1.9   |
| Olanzapine         | 1 0.9                 |                   |                   | 1 0.9   | 2 1.9   |
| Paliperidone       | 1 0.9                 |                   |                   | 1 0.9   | 2 1.9   |
| Pipamperone        | 1 0.9                 |                   |                   | 1 0.9   | 2 1.9   |
| Prazepam           | 5 4.6                 | 12 11.1           | 5 4.6             | 3 2.8   | 6 5.6   | 3 2.8   |
| Promethazine       | 2 1.9                 | 2 1.9             | 3 2.8             | 1 0.9   | 2 1.9   |
| Quetiapine         | 1 0.9                 |                   |                   | 1 0.9   | 2 1.9   |
| Risperidone        | 1 0.9                 |                   |                   | 1 0.9   | 2 1.9   |
| Trazodone          | 1 0.9                 |                   |                   | 1 0.9   | 2 1.9   |
| Sodium valproate   | 4 3.7                 | 1 0.9             | 2 1.9             | 3 2.8   | 4 3.7   |
| zuclopenthixol     | 3 2.8                 |                   |                   | 4 3.7   | 10.2   |
| zuclopenthixol (LA)| 2 1.9                 | 3 2.8             | 9 8.3             | 7 6.5   | 4 3.7   | 11 10.2 |
| Total              | 108 100               | 108 100           | 108 100           | 108 100 | 108 100 | 108 100 |

LA long acting.
choice drug in the non-secluded patients was noticed for secluded patients ($p = 0.075$, with $n = 12$ younger and $n = 2$ older physicians).

**Which drug preferences are most likely to be affected by a seclusion?**

In order to detect if a drug preference was significantly altered when considering seclusion status of the patient a McNemar test for binomial proportions for matched-pair data was performed. If we consider the drugs that were picked as number 1 and compare this preference between secluded and non-secluded patients then droperidol is more preferred in the secluded patients ($p = 0.022$) and lorazepam in the non-secluded patients ($p = 0.022$). If we consider preference as placing this drug in the top 3 we found that droperidol ($p = 0.003$) and zuclopenthixol long formula ($p = 0.039$) are preferred in secluded patients and olanzapine ($p = 0.012$) and quetiapine ($p = 0.006$) in non-secluded patients.

### Use of guidelines and monitoring for efficacy and safety

Guidelines are not frequently used. Only 29 respondents (26.9%) report the use of guidelines. Of these 29, 62.1% use local guidance or recommendations, 17.2% a recommendation issued by a national professional society or 20.7% a published guideline. The majority of respondents (97.2%) uses only clinical response evaluations to monitor the effect of the rapid tranquillisation. There is no use of physical monitoring.

### Discussion

Agitation is a regularly encountered clinical condition by psychiatrists as well as by emergency physicians since 64% of the respondents have up to ten cases per month in treatment and 21% up to twenty cases per month.

The results of this study show that there is no clear or systematic rationale for prescribing for acute agitation in Belgium. In this respect, variability in practice in Belgium is comparable to other countries [21]. This is the most important finding since considerable risks (use

### Table 3 Between group differences in non-secluded patients

| Nr 1 favoured product | Top 3 favoured products |
|-----------------------|-------------------------|
|                       | Psychiatrist (n = 71) | Emergency physician (n = 37) | Fisher’s exact p |
|                       |                       |                           |                     |
|                       | Psychiatrist (n = 71) | Emergency physician (n = 37) | Fisher’s exact p |
|                       |                       |                           |                     |
| Alprazolam LA          | 0 (0)                 | 0 (0)                     | –                    |
| Alprazolam             | 1 (1.4)               | 1 (2.7)                   | 1.000                |
| Aripiprazole           | 3 (4.2)               | 0 (0)                     | 0.55                 |
| Bromazepam             | 0 (0)                 | 0 (0)                     | –                    |
| Clonazepam             | 0 (0)                 | 0 (0)                     | –                    |
| Clorazepaat            | 2 (2.8)               | 2 (5.4)                   | 0.605                |
| Clozapine              | 17 (23.9)             | 4 (10.8)                  | 0.128                |
| Diazepam               | 0 (0)                 | 5 (13.5)                  | 0.004                |
| Droperidol             | 5 (7.0)               | 2 (5.4)                   | 1.000                |
| Escitalopram           | 0 (0)                 | 0 (0)                     | –                    |
| Haloperidol            | 3 (4.2)               | 4 (10.8)                  | 0.228                |
| Lorazepam              | 14 (19.7)             | 9 (24.3)                  | 0.625                |
| Midazolam              | 0 (0)                 | 2 (5.4)                   | 0.115                |
| Olanzapine             | 17 (23.9)             | 7 (18.9)                  | 0.631                |
| Paliperidone           | 0 (0)                 | 0 (0)                     | –                    |
| Pipamperone            | 0 (0)                 | 0 (0)                     | –                    |
| Prazepam               | 0 (0)                 | 0 (0)                     | –                    |
| Promethazine           | 0 (0)                 | 0 (0)                     | –                    |
| Quetiapine             | 5 (7.0)               | 0 (0)                     | 0.163                |
| Risperidone            | 2 (2.8)               | 0 (0)                     | 0.545                |
| Trazodone              | 0 (0)                 | 0 (0)                     | –                    |
| Sodium Valproate       | 0 (0)                 | 1 (2.7)                   | –                    |
| Zuclopenthixol         | 0 (0)                 | 0 (0)                     | –                    |
| Zuclopenthixol LA      | 2 (2.8)               | 0 (0)                     | 0.545                |

Fisher’s exact test was performed when one of the two groups had at least two counts (two-sided).
of physical restraint, cardiovascular severe side effects, higher likelihood of high dose prescribing and polypharmacy) are attached to prescribing in acute agitation without clear and evidence based rationale.

Antipsychotics are ranked most often first choice and benzodiazepines second choice when all respondents in the survey are considered. In non-secluded patients, preference is given to olanzapine, lorazepam and clozapine. In secluded patients, who arguably demonstrate higher degrees of agitation compared to non-secluded patients, clotiapine, olanzapine and droperidol are prescribed the most. The preference of droperidol is of particular interest since this drug has been banned from use in North America and the UK because of concerns over its cardiotoxicity, more specifically the significant lengthening of the QTc interval in certain patients [22]. Again, this finding illustrates the lack of international evidence based rationale in guiding the treatment of agitation. A recent consensus statement of the psychopharmacology workgroup of the American Association for Emergency Psychiatry [23] recommended antipsychotics—and in particular olanzapine or risperidone—as first-line management of acute agitation. However, this consensus statement does not differentiate patients according to their level of agitation, as is the case in our study. On the basis of a non-systematical review of the literature, Bak et al. [24] also advise for olanzapine and lorazepam, although the authors recommend to use lorazepam only in non-psychotic agitation. In addition, in a review of the literature in the period 1960–2000 by Battaglia et al. [25], it was found that most evidence for a safe and effective treatment of acute agitation was found for haloperidol, olanzapine and lorazepam. This recommendation is also supported in the NICE guideline on acute agitation [26].

The findings from our study point out that clinicians have a complex relationship with these guidelines. When they are asked to consider non-secluded and therefore mildly agitated patients, prescribing preferences are in line with published evidence. In contrast with this, when asked to consider secluded patients with evidently higher levels of agitation, preference is given to drugs with a higher risk profile, such as droperidol. This discrepancy highlights the need for evidence based guidelines that take into account the level of agitation and the potential side effects of the prescribed medication.

Table 4 Between group differences in secluded patients

| Nr 1 favoured product | Emergency physician (n = 71) | Fisher’s exact p | Emergency physician (n = 37) | Fisher’s exact p |
|-----------------------|-------------------------------|-----------------|-------------------------------|-----------------|
| Psychiatrist          | Brevoets et al. BMC Res Notes (2015) 8:218 Page 6 of 8 |
|                        | 0 (0)                         |                 | 1 (1.4)                      |                 |
| Alprazolam            | 0 (0)                         | 1 (2.7)         | 2 (2.8)                      | 4 (10.8)        |
| Aripiprazole          | 3 (4.2)                       | 1 (2.7)         | 1 (1.4)                      |                 |
| Bromazepam            | 0 (0)                         | 0 (0)           | 1 (1.4)                      |                 |
| Clonazepam            | 0 (0)                         | 0 (0)           | 1 (1.4)                      |                 |
| Cloxazolam            | 0 (0)                         | 0 (0)           | 1 (1.4)                      |                 |
| Clozapine             | 3 (4.2)                       | 1 (2.7)         | 10 (14.1)                    | 7 (18.9)        |
| Clopenthaxol          | 16 (22.5)                     | 7 (18.9)        | 31 (43.7)                    |                 |
| Diazepam              | 0 (0)                         | 6 (16.2)        | 6 (8.5)                      | 20 (54.1)       |
| Droperidol            | 13 (18.3)                     | 3 (8.1)         | 21 (39.4)                    | 11 (29.7)       |
| Escitalopram          | 0 (0)                         | 0 (0)           | 0 (0)                        |                 |
| Haloperidol           | 3 (4.2)                       | 1 (2.7)         | 10 (14.1)                    | 14 (37.8)       |
| Lamotrigine           | 0 (0)                         | 0 (0)           | 0 (0)                        |                 |
| Lorazepam             | 6 (8.5)                       | 8 (21.6)        | 38 (53.5)                    | 14 (37.8)       |
| Midazolam             | 0 (0)                         | 2 (5.4)         | 34 (47.9)                    | 9 (24.3)        |
| Olanzapine            | 17 (23.9)                     | 6 (16.2)        | 0 (0)                        |                 |
| Prazepam              | 0 (0)                         | 0 (0)           | 1 (1.4)                      | 0 (0)           |
| Promethazine          | 0 (0)                         | 0 (0)           | 1 (1.4)                      | 3 (8.1)         |
| Quetiapine            | 3 (4.2)                       | 0 (0)           | 12 (16.9)                    | 0 (0)           |
| Risperidone           | 0 (0)                         | 0 (0)           | 2 (2.8)                      | 1 (2.7)         |
| Zuclopenthixol        | 0 (0)                         | 0 (0)           | 4 (5.6)                      | 0 (0)           |
| Zuclopenthixol LA     | 7 (9.9)                       | 0 (0)           | 22 (31.0)                    | 0 (0)           |
| Sodium Valproate      | 0 (0)                         | 1 (2.7)         | 2 (2.8)                      | 1 (2.7)         |
| Paliperidone          | 0 (0)                         | 0 (0)           | 1 (1.4)                      | 0 (0)           |
| Pipamperone           | 0 (0)                         | 0 (0)           | 1 (1.4)                      | 1 (2.7)         |

Fisher’s exact test was performed when one of the two groups had at least 2 counts (2-sided).
of agitation, the compliance with guidelines disappears and potent sedative drugs as clotiapine and droperidol emerge as a preferred choice.

It should be noted that zuclopenthixol is not a drug of choice for agitated patients since it does not meet the requirements of a drug used in rapid tranquillisation (i.e. onset of action within 20–30 min, maximum plasma concentration within 2 h, short half-life). However, the long acting form of zuclopenthixol is found to be well-favored, both in non-secluded as in secluded patients. This is not in line with earlier mentioned recent recommendations found in the literature [23, 24, 27] where long acting drugs have no place in the acute treatment of agitation and thus there is a clear need for education. The observation that some medications (e.g. escitalopram) are used which are not considered suitable for managing acute agitation is also of importance in this light.

An interesting finding is that a comparison between type of medical specialist produced significant differences in prescription preferences. Most notably, emergency physicians prefer benzodiazepines most, both in secluded and in non-secluded patients. The analysis of these responses on the level of individual drugs shows that (1) no specific preference for benzodiazepines with shorter half life could be found (midazolam as well as diazepam are reported) and (2) that specifically psychiatrists prefer antipsychotics as quetiapine (in all patients), olanzapine (in patients with higher levels of agitation) and long acting zuclopenthixol the most. This gives evidence to support the hypothesis that both types of specialists use different strategies to treat acute agitation. To our knowledge, this distinction is never made in earlier prevalence studies although it seems relevant from our data to do so. It is known that psychiatrists and emergency physicians have a different education with respect to psychotropic medication or use these drugs in other indications which may lead to a bias in selection preference. Moreover, the content of the hospital formulary may differ between general hospitals and psychiatric hospitals, which could in turn also lead to the selection of different treatments. It can also be argued that the purpose of rapid tranquillisation for the psychiatrist might be to effectively sedate the patient but without hampering further diagnostic actions, whilst an emergency doctor is primarily focused on controlling the disruptive behaviour. Finally, physicians—in Belgium—are approached with different pharmaceutical information by different pharmaceutical companies. It can be postulated that this practice also has an effect on which drug is prescribed, certainly in the context of our finding that most respondents never use any published guideline.

The age of the prescribing physician also plays an important role. Older physicians prefer significantly more the use of the long acting form of zuclopenthixol when compared to their younger peers (in secluded patients). This could also be interpreted as an effect of education or changes in information strategies from pharmaceutical companies.

An explanation for our finding of a sparse use of monitoring—at least for assessment of efficacy of a treatment—can be found in a recent systematic review by Zeller and colleagues who reported a similar observation [28]. The authors hypothesize that, although agitation is a common behavioural emergency, there is a lack of easy-to-administer instruments that could improve treatment quality or predict treatment effects.

Our study has several limitations. The response rate is low, the definition of agitation that was used is not a clear clinical definition and there were no questions on how medication was delivered to the patient (per os, intramuscularly, intravenously).

**Conclusion**

There is no clear or systematic rationale for prescribing for acute agitation in Belgium. Practice in treating acute agitation shows a complex relation with published evidence and guidelines. The level of agitation in patients and the type of physician prescribing the first pharmaceutical treatment both are clearly important variables and should be implemented in further research designs. A variety of causes can be put forward to explain this difference between both groups of physicians and this also warrants further research.

The high prevalence of the non-recommended use of zuclopenthixol acetate in the psychiatrist group raises concern and should be taken into account in future medical education. Moreover, it is of great concern that there is a substantial lack in the existence and in the use of assessment tools that measure the effect and safety of a treatment—preferably directly in the moment and in the patient and not post hoc by means of a measurement scale by a caregiver.

Note: Availability of psychotropic drugs outside Belgium

Certain drugs mentioned in this study are bot available or in use in countries outside Belgium. Clotiapine is a dibenzothiazepine with ATC (Anatomical Therapeutic Chemical Classification) N05AH06, Bromazepam is a benzodiazepine with ATC (Anatomical Therapeutic Chemical Classification). N05BA08 and pipamperone is a bipiperidine with ATC (Anatomical Therapeutic Chemical Classification) N05AD05.

**Authors’ contributions**

CB, BS and MM conceptualized the research idea. CB, BS and MM designed the study. CB collected the clinical data. CB, MM, BS and ER analyzed the data and
wrote the first draft of the manuscript. MM and BS supervised the research project and critically revised the manuscript. All authors contributed to and have approved the final manuscript.

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**Compliance with ethical guidelines**

The authors declare that they have no conflict of interest.

**Competing interests**

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