

V. Fernández García  
de las Heras  
N. Mendiola Muñoa  
M. Ramírez Reinoso  
J. Valle Fernández

# Review of aggression management in an emergency setting

Psychiatry Service  
Hospital Universitario de La Princesa  
Madrid, Spain

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Aggression management is a challenge most clinicians have to face, especially in an emergency service. Managing behavioral emergencies is a usual problem for mental health staff that requires making quick decisions in situations in which the patient and the staff security is of priority. In addition there is growing development and complexity in pharmacological treatments. That is why there is an increasing interest to provide guidelines and structured policies based on clinical trial data.

**Key words:**

Agresion. Management. Behavioral emergencies.

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## Revisión del manejo de la agresividad patológica en situación de urgencia

El manejo de la agresividad es un reto con el que con frecuencia se encuentran los servicios médicos, especialmente en el marco de la urgencia. Abordar la constelación de trastornos de conducta que ésta puede generar es un problema frecuente para los profesionales de salud mental, que requiere la toma de decisiones rápidas en situaciones en las cuales la seguridad del paciente y del personal es la prioridad. A esto se añade la complejidad y el desarrollo creciente de los tratamientos farmacológicos. De ahí que exista un interés renovado en intentar determinar estrategias físicas y farmacológicas sustentadas en las investigaciones científicas actuales que permitan establecer un marco apropiado de actuación.

**Palabras clave:**

Agresividad. Manejo. Urgencias. Trastornos de conducta.

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**Correspondence:**

Victoria Fernández García de las Heras  
Servicio de Psiquiatría  
Hospital de La Princesa  
Diego de León, 62  
28006 Madrid, Spain  
E-mail: vicfgh@latinmail.com

## INTRODUCTION

Aggressiveness is a universal instinctive behavior. It lacks etiology in the medical sense, since it is not morbid. There are a series of unavoidable difficulties from the methodological point of view when dealing with the subject of pathological aggressiveness or violence empirically: heterogeneous and multiple etiology, not always psychiatric; inherent problems when managing investigations in aggressive populations; the combination of drugs that are usually necessary for adequate control of aggressive behaviors; varied terminology whose limits have not been well-defined as of yet and that are used indistinctly in the literature<sup>1</sup>.

Due to all this, predicting with certainty which patients will have violent behaviors is not clinically possible<sup>2,3</sup>. However, it is possible to identify risk factors in order to establish an estimation based on evidence of the probability of aggressiveness<sup>4</sup>. On the other hand, and in spite of the difficulties mentioned, adequate management of aggression/agitation, especially in the context of emergency, is an essential requirement for the patient's and staff's safety.

The studies show that serious mental patients, especially during acute decompensations of their disease, run an increased risk of being seen and evaluated as a psychiatry emergency<sup>5,6</sup>.

Knowledge of the physical and pharmacological actions recommended, based on the existing studies, support with sufficient guarantee an especially important part in our daily practice.

## EPIDEMIOLOGY

Approximately 10% of the patients admitted to psychiatric units show violence towards others just before their admission<sup>7</sup>. It is interesting to mention that prevalence of agitation and aggression is much greater among the patients

with neuropsychiatric disorders (post-traumatic brain damage, dementias, etc.) than among patients hospitalized with chronic psychiatric disorders<sup>8,9</sup>.

Four clinical characteristics contribute significantly to the risk of violence between persons with a serious mental disease: acute and scarcely controlled disease<sup>10,11</sup>, non-therapeutic compliance<sup>12</sup>, substance abuse<sup>13</sup> and past history of violent behavior<sup>10,14</sup>. Each one of these is an independent risk factor of aggression in psychosis. However, these traits often coincide and act synergically both for appearance as well as repetition of violent behaviors.

There are authors who state that it is almost impossible to predict violent behaviors in patients on the bases of the symptoms, isolated risk factors having been demonstrated to be much greater in regards to the statistical assessment of potential risk of violence. Thus, they state that in a clinical interview, the best that can be expected is that the clinician uses identified risk factors, in order to make an estimation based on the evidence of the possibility of violent behaviors<sup>15</sup>.

The likelihood of violent behavior is greater in schizophrenic patients with affective disorders and substance abuse versus persons without psychiatric diagnosis. Post-traumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD) also increase the likelihood of aggression<sup>16-18</sup>. The diagnostic groups that may most often have risk of aggression in the initial phase of admission are manic patients. This group is followed by schizophrenic and schizoaffective patients in regards to the first eight days of hospitalization. Principally, the objects of the patient's violence are most likely family members, friends or relatives (89.3%)<sup>1</sup>.

Recurrent and transitory aggressiveness must be distinguished. Transitory and recurrent violence may differ in cause, management and social consequences. In this sense, a small number of patients (those who have recurrent aggressiveness) may be responsible for most of the incidents. The most frequent diagnoses among patients with recurrent aggressive behaviors are those of schizophrenia or psycho-organic syndrome in men and personality disorder and lack of control of impulses in women<sup>1</sup>.

#### **MANAGEMENT OF ACUTE AGGRESSIVENESS. ASSOCIATION AND DIAGNOSIS OF THE AGGRESSIVENESS PATIENT**

The family members, friends or work colleagues should be interviewed because patients with aggressive behaviors, on the contrary to their families, tend to minimize the presence or importance of the disorder. In addition, to develop a treatment plan, the clinician should find out in what context the aggressiveness develops from the patient and also based on his/her setting.

Essential information includes the mental state of the patient before the aggressive behavior, the precipitating factors, physical and social setting, ways in which the violent behaviors can be decreased, and primary and secondary gains that may be related to it.

If the agitation or aggressiveness appears in the context of a psychiatric disorder, a detailed psychiatric history of the individual and his/her family should be obtained.

If an organic disease is suspected, possible neurological symptoms or signs should be reviewed and a physical examination performed. Complementary laboratory test based on the information obtained from the clinical history must also be considered.

### **NON-PHARMACOLOGICAL TREATMENT**

#### **Why are emergency guidelines necessary?**

An extensive review on restraint and seclusion methods<sup>19</sup> suggested that they worked in a limited way, preventing harm and reducing agitation. However, it described noxious effects in the patients, who perceive such interventions as coercive and traumatic. This perception is reinforced by a publication in 1990<sup>20</sup> in which great variability was demonstrated in the use of restraint and seclusion, more in function of the institutional culture than on the patient's individual characteristics. The controversy increased in relationship with several cases of deaths in patients with restraint and seclusion.

It is in this context that documents obtained from the participation of a group of experts<sup>21</sup> are elaborated to define the following elements: the threshold to conduct emergency interventions; the reach of the assessment of different emergency levels; guideline principles when selecting the appropriate physical and pharmacological strategies and interventions at different diagnostic confidence levels.

There are other documents such as that of the American Psychiatric Nurses Association<sup>22,23</sup> whose objective is to guarantee that both measurements (restraint and seclusion) are duly used, the least frequently possible, and only when less restrictive methods have been considered and cannot be applied. To do so, a series of fundamental points are mentioned, among which, the following stand out: constant dialogue among the different staff members; work groups; defining the action field and personnel roles; real objectives; incorporating the families, patients and guideline principles of the personnel to the action policy; confidence and reinforcement attitude regarding the times when the use of restraint or seclusion is necessary; defined action programs and protocols.

## Use of mechanical restraint

### Introduction

It is used in 6% of hospitalized psychiatric patients; between 51% and 59% in the elderly residences<sup>24</sup>; in 23% of the cases of child psychiatric hospitalizations<sup>25</sup>; and the prevalence is found at 30% when psychiatric patients seen in an emergency service are observed<sup>26</sup>.

In a review of the Cochrane Library on mechanical restraint and seclusion applied to severe cases of mental disease<sup>27</sup>, no controlled studies that evaluated the utility of these methods were found. However, the serious adverse effects that this practice produces are collected in the literature, so that the development of new strategies that are less dangerous and harmful is suggested.

### Definition of movement restriction and seclusion

According to the Joint Commission of the Accreditation of Health Care Organization (JCAHO)<sup>28</sup>, restriction is the use of physical or mechanical procedures aimed at limiting movements of part or all the body of a patient, in order to control the patient's physical activities and protect the patient from inflicting injuries on him/herself or others. Seclusion is understood to be confinement of a patient, alone in a room, preventing him/her from leaving it for a limited time period.

### When to use mechanical restraint

Only when less restrictive measures have failed and an unpredictable severely aggressive or destructive behavior places the patient or others in imminent danger. More than 80% of the patients are managed without the need for parenteral medication, restraint or seclusion<sup>21</sup>.

### Aspects related to personnel

Three groups of personnel are involved in the restraint process:

- Someone who makes the decision to initiate the process. The most appropriate personnel members to make the decision and carry out the later appropriate evaluation are psychiatrists or nurses, preferably with experience or preparation in psychiatric emergencies.
- A group of team members physically place the mechanical restraint: the members that are considered most adequate to carry out this task are the nursing team and trained security personnel.
- A face to face evaluation is performed to assess the need to maintain the restraint.

### Duration of the episode

The maximum time established for restraint and/or seclusion is 8 h (one shift). If the clinical situation allows it, it could be shortened as much as possible. If it is necessary to prolong it, this should be expressly authorized in each shift by those responsible in each case. The time limit during which an indication of restraint and/or seclusion can be prolonged is 72 h. Once this extreme margin is exceeded, the patient should be freed. Any other indication of restraint must be assessed newly and the procedure must be initiated from the beginning.

### Guarantee the observation

Indication of restraint and/or seclusion increases the tasks, given the general seriousness of the patients it is applied to. The medical personnel should perform the first observation, preferably in the first hour, always before 3 h. Within the nursing staff, any member of the staff who attends to the service can perform the visit, which must be done to these patients at least every 15 min. The patient's condition, that of the restraints and any other need that may arise should be reviewed<sup>29</sup>.

### Use of medication while mechanical restraint is maintained

There is a division on whether to offer oral medication or not in this situation. Parenteral medication is not recommended. However, if the patient continues to be violent and agitated, in spite of the mechanical restraint, the experts<sup>21</sup> are in favor of using parenteral medication combined with restraint, although the use of oral medication would also be considered. The objective of these interventions would be to minimize the time and/or complications of the restraint.

If this is not enough to be able to reduce the patient's agitation or violent behavior, it is sometimes necessary to reduce all environmental stimuli as much as possible. In these cases, the patient should be secluded if the physical facilities of the service allow for it.

The characteristics of the physical and human setting have a powerful effect that calms and prevents, or worsens and precipitates manifestations of the violence. Regarding this setting, different articles are relevant for the hypotheses formulated. However, all are descriptive and none have a completely controlled design. As the data collection, measurement and analysis methods are so varied, it is impossible to incorporate the results, so that firm conclusions based on the evidence cannot be drawn<sup>30,31</sup>.

## PHARMACOLOGICAL TREATMENT

Pharmacological treatment should only be initiated when the patients do not respond to behavioral or environ-

mental interventions. Treatment should be started with low doses, evaluating the side effects and maintaining it the least time possible.

Few double blind studies have approached the pharmacological treatment of aggressiveness. The available studies have been performed to determine the efficacy of certain drugs in psychiatric disorders in which aggressiveness is frequent<sup>32</sup>.

## Benzodiazepines

Although they have great prestige, especially in the medical-surgical section, they are not the best solution to resolve the emergency situation. First, their action is faster orally, and it is rare that an agitated patient would accept this administration route. In the second place, they may depress the CNS respiratory center.

There is a benzodiazepine that has demonstrated rapid i.m. absorption: lorazepam, and it is recommended as an option in these cases. Of the 24 studies reviewed by Allen<sup>21</sup>, comparing different medications in the treatment of acute aggressiveness, when haloperidol and lorazepam were compared as a single treatment, the latter was superior in decreasing the aggressiveness score and on the global evaluation scale. Several studies<sup>33,34</sup> even report that the combination of haloperidol and lorazepam is superior to lorazepam only in the management of agitation. Unfortunately, this formulation is not marketed in Spain.

The remaining benzodiazepines are absorbed more slowly by the i.m. route, some painfully (e.g.: diazepam), others with doubtful efficacy, since they need to be hydrolyzed in the stomach (oral route) in order for the active metabolite to act (e.g., clorazepate dipotassium).

## Neuroleptics

They are the safest drugs to control agitation<sup>35</sup>, even with strict precautions in elderly subjects. Their undesirable effects are anticholinergics, postural hypotension, excessive sedation, extrapyramidal symptoms and, in some cases, epileptic crisis as they decrease the seizure threshold. The last possible action is that which advises against using neuroleptics in alcoholics undergoing alcohol deprivation.

The neuroleptics begin to act during the first 20 min of their administration and, in general, are able to control the agitation and/or violence situation in a maximum period of 6 h. The use of high potency and low profile of side effects neuroleptics is preferable. The neuroleptic pattern is, in this case, a butyrophenone: haloperidol, whose main disadvantage is extrapyramidal symptoms. Chlorpromazine, having less sharp action but greater sedative power, is also frequently used. Its disadvantages regarding haloperidol are: greater an-

ticholinergic and hypotensive action. Blood pressure, heart and respiratory rate must always be controlled. Sedation is aimed at, however, the patient should not sleep. Once achieved, the total dose needed is calculated and then this fractionated dose will be administered in three doses per day.

## Typical antipsychotics

Typical antipsychotics, especially those of high potency, have had fundamental importance in the treatment of aggressiveness, especially in the context of active psychosis. There is strong evidence in favor of their use based on a long and satisfactory history of intramuscular administration in the management of acute aggressiveness<sup>36</sup>. Until a few years ago, haloperidol was the most frequently prescribed antipsychotic medication, also being the one that had the best evidence in the treatment of aggressiveness. Haloperidol and related antipsychotics have sedative and antipsychotic effects, although it is not clear if they have a selective target independent of these properties. It must be understood that high doses of neuroleptics may worsen aggressiveness, probably increasing akathisia<sup>37</sup>. One review of several studies that examined the dose of haloperidol for acute psychosis did not observe additional beneficial effects once a dose of 10 to 16 mg i.m. had been administered<sup>38</sup>.

## Atypical antipsychotics

Due to their specific action mechanism, they have less incidence of side effects, their efficacy in long term treatments having been demonstrated on the other hand. Regarding their effect on aggressiveness, they seem to decrease hostility and physical aggressions, at least in long duration treatments. This quality is especially clear with clozapine, but the literature suggests that other atypical antipsychotics, such as risperidone, share this effect<sup>39</sup>.

It is hypothesized that the greater tendency to block the 5-HT<sub>2</sub> receptor together with a lesser blockage of the dopaminergic receptors (D<sub>2</sub>) define the specific profile of atypical antipsychotics. Recent studies verify that the best predictor of atypicity is low affinity and rapid dissociation of the D<sub>2</sub> receptor (so that it rapidly separates to permit normal neurotransmission of dopamine)<sup>40</sup>.

## Clozapine

When clozapine was first available in the USA, the clinicians observed a decrease in restraint and seclusion rates and the use of emergency medications. The consistency of this observation through various studies raises the question of whether clozapine has a specific antiaggressive effect. Studies in this sense examine hostility and psychosis scores, observing the limited relationship between the changes of score of both subscales, suggesting that clozapine could have a se-

lective antiaggressive effect<sup>41</sup>. These studies were mainly performed with schizophrenic patients, although it also seems to have demonstrated a reduction in aggressiveness in non-psychotic patients, such as in borderline personality disorders.

In several uncontrolled studies reviewed by Glazer and Dickson<sup>42</sup>, it has been demonstrated that its use is related with decrease of the frequency of the use of mechanical restraint and seclusion and with the decrease in the number of re-hospitalizations of patients hospitalized due to this type of behaviors.

### Risperidone

Several studies find an effect on aggressiveness that is superior to haloperidol<sup>39</sup>, a similar efficacy to the conventional neuroleptics, aggressiveness improving in patients with schizophrenia<sup>43</sup> and a significant decrease in restraint and seclusion before and after having initiated treatment with risperidone<sup>44</sup>.

Except for clozapine, risperidone has shown better evidence in antiaggressive efficacy in middle-long term treatments<sup>39</sup>. The availability of risperidone in liquid form is an advantage when choosing between drugs for acute management of agitation. The appearance of the i.m. presentation must also be taken into account, although with a different patient target profile.

### Olanzapine

An analysis of multicenter clinical trials shows similar efficacy between haloperidol and olanzapine in the treatment of agitation and/or aggressiveness, with improvement in the profile of side effects such as extrapyramidal symptoms (EPS) and akathisia. Thus, in a double placebo study that compared intramuscular administration of olanzapine and that of haloperidol in acute treatment of aggressiveness, a similar efficacy was found with the difference that acute dystonias did not appear with olanzapine versus 7% in those treated with haloperidol<sup>45</sup>.

### Ziprasidone

The studies suggest an effectiveness of the i.m. formula comparable to that of haloperidol in terms of rapid sedation and good tolerability by the patients as the incidence of EPS decreases<sup>46,47</sup>. The sedative effect of ziprasidone is dose-dependent, providing the best results with intramuscular doses of 10 and 20 mg<sup>48</sup>.

## Therapy combined with benzodiazepines

The expert consensus guideline<sup>21</sup> recommends the combination of benzodiazepines with conventional or atypical

antipsychotics in cases of agitation in patients where schizophrenia or mania is suspected. This was also one of the priority options in the case of psychotic depression. If parenteral administration is necessary, either benzodiazepines alone or in combination with a typical antipsychotic should be chosen (schizophrenia, psychotic depression, mania or, if there is provisionally no diagnosis).

## CONCLUSIONS

The present organization of the treatment of psychiatric patient from the basically out-patient setting has meant a reduction in the number of admissions<sup>49</sup> in acute units, however, on the other hand, it has led to greater demand and exactness in the interventions of the emergency service, in regards to psychodrugs and to the different non-pharmacological and behavioral approaches.

Conventional antipsychotics involve the pattern of gold standard pharmacological treatment in the treatment of aggressiveness. Haloperidol, as paradigmatic representative of this group, has not only been the most prescribed antipsychotic until a few years ago, but there are also many studies that support its proven indication in agitation.

Increasing experience with atypical antipsychotics and appearance of i.m. presentations stress its profile as a safe and effective alternative to the typical ones, with the comparative advantage of limited side effects.

The benzodiazepine group continues to be shown, either alone or combined with antipsychotics, as an essential element.

In regards to mechanical restraint and non-pharmacological measures, we stress the relevance of their adequate indication and administration by trained personnel as a very useful complement to preserve the personnel's and patient's safety in situations of manifest aggressiveness.

To continue assessing and clarifying the specific weight of each intervention or their combination, more studies and new proposals that serve to smooth out and improve the still existing methodological inaccuracies are necessary.

## REFERENCES

1. Citrome L, Volavka J. Aggression (on line). Febrero 2002 (date y access October 21, 2002). Available in URL; <http://www.emedicine.com/med/topic3005.htm>.
2. Buchanan A, Leese M. Detention of people with dangerous severe personality disorders: a systematic review. *Lancet* 2001; 358:1955-9.
3. Hughes D. Suicide and violence assessment in psychiatry. *Gen Hosp Psychiatry* 1996;18:416-21.
4. Nijman H, Merckelbach H, Evers C, Palmstierna T, Campo AJ. Prediction of aggression on a locked psychiatric admission ward. *Acta Psychiatr Scand* 2002;105:390-5.

5. Davis S. Violence by psychiatric inpatients: a review. *Hosp Community Psychiatry* 1991;42:585-90.
6. McNeil DE, Binder RL. The relationship between acute psychiatric symptoms, diagnosis, and short-term risk of violence. *Hosp Community Psychiatry* 1994;45:133-7.
7. Tardiff K, Swelliam A. The occurrence of assaultive behavior among chronic psychiatric inpatients. *Am J Psychiatry* 1982; 139:212-5.
8. Elliot FA. Violence: the neurologic contribution: an overview. *Arch Neurol* 1992;49:595-603.
9. Hales RE, Yudofsky SC, Talbott JA, editores. *The American Psychiatric Press Textbook of Psychiatry*, 3<sup>rd</sup> ed. Washington: American Psychiatric Press, 1999.
10. McNeil D. Correlates of violence in psychotic patients. *Psychiatr Ann* 1997;27:683-90.
11. Taylor PJ. Schizophrenia and the risk of violence. En: Hirsh SR, Weinberger DR, editores. *Schizophrenia*. Oxford (England): Blackwell Science, 1995; p. 163-83.
12. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. *Schizophr Bull* 1995;21:419-29.
13. Swanson J, Holzer C, Gant V, et al. Violence and psychiatric disorder in the community: evidence from the epidemiologic catchment area surveys. *Hosp Community Psychiatry* 1990; 41:761-70.
14. Harris GT, Rice ME. Risk appraisal and management of violent behavior. *Psychiatric Serv* 1997;48:1168-76.
15. Hughes DH, Kleespies PM. Treating aggression in the psychiatric emergency service. *J Clin Psychiatry* 2003;64(Suppl. 4):10-5.
16. Yehuda R. Managing anger and aggression in patients with post-traumatic stress disorder. *J Clin Psychiatry* 1999;60(Suppl. 15): 33-7.
17. Lavine R. Psychopharmacological treatment of aggression and violence in the substance using population. *J Psychoactive Drugs* 1997;29:321-9.
18. Hollander E. Managing aggressive behavior in patients with obsessive-compulsive disorders and borderline personality disorder. *J Clin Psychiatry* 1999;60(Suppl. 15):38-44.
19. Fisher WA. Restraint and seclusion: a review of the literature. *Am J Psychiatry* 1994;151:1584-91.
20. Way BB, Banks SM. Use of seclusion and restraint in public psychiatric hospitals: patient characteristics and facility effects. *Hosp Community Psychiatry* 1990;41:75-81.
21. Allen MH, Currier GN, Hughes DH, Reyer-Harde M, Docherty JP, Ross RW. The Expert Consensus Guideline Series. Treatment of behavioral emergencies. *Postgrad Med* 2001(spec No):1-88.
22. American Psychiatric Nurses Association (2000). Position statement on the use of seclusion and restraint. Available in URL; <http://www.apna.org>.
23. American Psychiatric Nurses Association (2003). Learning from each other: success stories and ideas for reducing restraint/seclusion in behavioral health. Available in URL; <http://www.apna.org>.
24. Tinetti ME, Liu WL, Ginter SF. Mechanical restraint use among residents of skilled nursing facilities: prevalence, patterns, and predictors. *JAMA* 1991;265:468-71.
25. Miller D, Walker MC, Friedman D. Use of holding technique to control the violent behavior of seriously disturbed adolescents. *Hosp Community Psychiatry* 1989;40:520-4.
26. Dabrowski S, Frydman L, Zakowska-Dabrowska T. Physical restraint in Polish psychiatric facilities. *Int J Law Psychiatry* 1986; 8:369-82.
27. Sailas E, Fenton M. Seclusion and restraint for people with serious mental illness (Cochrane review). The Cochrane Library, issue 4, 2002. Oxford.
28. Joint Commission on the Accreditation of Healthcare Organizations. *Comprehensive Accreditation Manual for Hospitals (CMAH)*. Available in URL; <http://www.jcaho.org>.
29. US Department of Health and Human Services, Health Care Financing Administration. *Hospital Conditions of Participation for Patient's Rights*. 42CFR 482.13. Baltimore, MD: HCFA; 1999. Disponible en URL; <http://www.hcfa.gov/quality/4b2.htm>.
30. Royal College of Psychiatrist. Management of imminent violence: clinical practice guidelines to support mental health services. College Research Unit. Occasional paper OP41. London, 1998.
31. Wright S. Control and restraint techniques in the management of violence in inpatient psychiatry: a critical review. *Med Sci Law* 2003;43:31-8.
32. McAllister-Williams RH, Ferrier IN. Rapid tranquilisation: time for a reappraisal of options for parenteral therapy. *Br J Psychiatry* 2002;180:485-9.
33. Battaglia J, Moss S, Rush J, et al. Haloperidol, lorazepam, or both for psychotic agitation? A multicenter, prospective, double-blind, emergency study. *Am J Emerg Med* 1997;15:335-40.
34. Biernek SA, Ownby RL, Penlaver A, et al. A double-blind study of lorazepam versus the combination of haloperidol and lorazepam in managing agitation. *Pharmacotherapy* 1998;18:57-62.
35. Buckley PF. The role of typical and atypical antipsychotic medications in the management of agitation and aggression. *J Clin Psychiatry* 1999;60(Suppl. 10):52-60.
36. Allen MH. Managing the agitated psychotic patient: a reappraisal of the evidence. *J Clin Psychiatry* 2000;61(Suppl. 14): 11-20.
37. Kamin J, Manwani S, Hughes D. Extrapyramidal side effects in the psychiatric emergency service. *Psychiatr Serv* 1999;50: 1553-4.
38. Baldessarini RJ, Cohen BM, Teicher MH. Significance of neuroleptic dose and plasma level in the pharmacological treatment of psychosis. *Arch Gen Psychiatry* 1988;45:79-91.
39. Czobor P, Volavka J, Meibach RC. Effect of risperidone on hostility in schizophrenia. *J Clin Psychopharmacol* 1995;15:243-9.
40. Seeman P. Atypical antipsychotics: mechanism of action. *Can J Psychiatry* 2002;47:27-38.
41. Citrome L, Volavka J, Czobor P, Sheitman B, Lindenmayer JP, McEvoy J, et al. Effects of clozapine, olanzapine, risperidone and haloperidol on hostility among patients with schizophrenia. *Psychiatr Serv* 2001;52:1510-4.
42. Glazer WM, Dickson RA. Clozapine reduce violent and persistent aggression in schizophrenia. *J Clin Psychiatry* 1998;58(Suppl. 3): 8-14.
43. Buckley PF, Ibrahim Zy, Singer B, Orr B, Donenwirth, Brar P. Aggression and schizophrenia: efficacy of risperidone. *J Am Psychiatry Law* 1997;25:173-81.
44. Chengappa KNR, Levine J, Ulrich R, et al. Impact of risperidone on seclusion and restraint at a state psychiatric hospital. *Can J Psychiatry* 2000;45:827-32.
45. Wright P, Birkett M, David SP, et al. Double-blind, placebo-controlled comparison of intramuscular olanzapine and intramus-

- cular haloperidol in the treatment of acute agitation in schizophrenia. *Am J Psychiatry* 2001;158:1149-51.
46. Brook S, Lucey JV, Gunn KP, for the Ziprasidone I. M. Study Group. Intramuscular ziprasidone compared with intramuscular haloperidol in the treatment of acute psychosis. *J Clin Psychiatry* 2000;61:933-41.
47. Daniel D, Potkin S, Reeves K, Swift R, Harrigan E. Intramuscular ziprasidone 20 mg is effective in reducing acute agitation associated with psychosis: a double-blind randomized trial. *Psychopharmacology* 2001;155:128-34.
48. Lesem MD, Zajecka JM, Swift RH, et al. Intramuscular ziprasidone, 2 mg versus 10 mg, in the short-term management of agitated psychotic patients. *J Clin Psychiatry* 2001;62:12-8.
49. Farnham FR, James DV. «Dangerousness» and dangerous law [comment]. *Lancet* 2001;358:1926.