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**IL PAZIENTE AGITATO IN PRONTO SOCCORSO:
MEDICI D'URGENZA E PSICHIATRI A CONFRONTO**

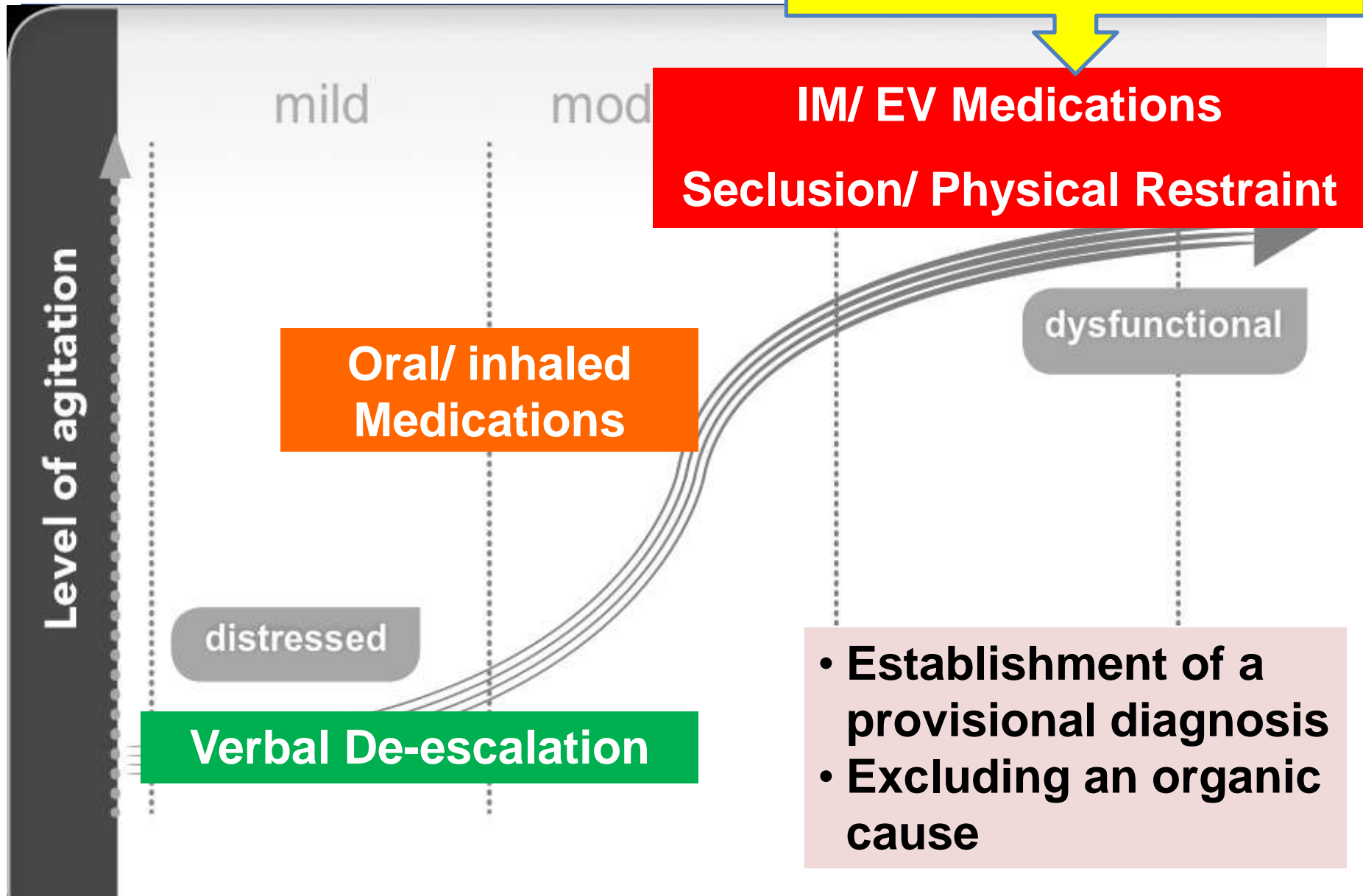
I Trattamenti Psicofarmacologici: Proviamo a Mettere Ordine?

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Agitation: the Continuum



Rapid Tranquilisation in Acute Behavioral Emergencies

TIMING

- **Parenteral medications in a stepwise approach.**
- **Calm/lightly sedate the patient.**
- **Reduce the risk to self and/or others.**
- **Allow a thorough psychiatric evaluation.**
- **Allow comprehension and response to spoken messages.**

The Psychopharmacology of Agitation: Consensus Statement of the American Association for Emergency Psychiatry Project BETA Psychopharmacology Workgroup

Table. Medications recommended in the treatment of agitation.

Wilson et al, West J Emerg Med. 2012;13(1):26–34.

	Initial dose, mg	Tmax*	Can repeat†	Maximum dose (per 24 hours), mg
Oral medication				
Risperidone	2	1 h	2	6
Olanzapine	5–10	6 h	2	20
Haloperidol‡	5	30–60	15 min	20
Lorazepam	2	20–30	2	12
Intramuscular medication				
Ziprasidone	10–20	15	10 mg q 2 h, 20 mg q 4 h	40
Olanzapine	10	15–45	20 min	30
Aripiprazole	9.75	1 h	2	30
Haloperidol‡	5	30–60	15 min	20
Lorazepam	2	20–30	2	12
Intravenous medication				
Haloperidol§	2–5	Immediate	4	10§

† Likely to cause higher incidence of extrapyramidal side effects than other recommended drugs.

§ Administering haloperidol intravenously increases risk of QT prolongation. Therefore, avoid if possible, especially in patients with borderline QT or taking other medication that can prolong QT. If given intravenously, limit dose and provide cardiac monitoring.

QT Lungo e Aritmie – Nota GAZZETTA UFFICIALE 13/3/07

AIFA 28/2/07: Modifica degli stampati di specialità medicinali

- **Aloperidolo, Droperidolo, Pimozide:**

- ✓ **Controindicazioni:** malattie cardiache clinicamente significative; prolungamento QTc; storia familiare di aritmie o TdP; ipopotassiemia non corretta; concomitante uso di farmaci determinanti prolungamento QTc.

- ✓ **Avvertenze speciali e precauzioni:** effettuare ECG di base e monitoraggio; ridurre dosaggio in caso di prolungamento QTc e sospendere in caso di >500 ms; controllo periodico elettroliti; evitare co-terapia con altri neurolettici.

SERENASE: Modifica Scheda Tecnica, 2011

- ✓ **Il rischio di prolungamento dell'intervallo QT e/o di aritmie ventricolari può aumentare con dosi elevate...o quando il medicinale è somministrato per via parenterale.**
- ✓ **SERENASE non deve essere somministrato per via endovenosa, in quanto la somministrazione endovenosa di aloperidolo è stata associata ad un maggiore rischio di prolungamento del tratto QT e di Torsione di punta.**

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- **Regardless of the true clinical risk, however, it seems prudent for physicians to avoid intravenous administration of haloperidol...**
- **When haloperidol must be administered intravenously, the dose should be limited to 5 to 10 mg/day and administered in conjunction with continuous ECG monitoring.**

II Generation IM Antipsychotics: Aripiprazole, Olanzapine, Ziprasidone

- **Indicated only in schizophrenia and mania (ARP, OLZ), and schizophrenia (ZPS)**
- **Aripiprazole 9.75 mg: effective and safe**
- **Ziprasidone 10 mg: same warning as haloperidol for QTc interval prolongation**
- **Olanzapine 10 mg:**
 - **12%: 20 mm Hg hortostatic drop**
 - **OLZ + BDZ: should be avoided (risk of respiratory depression)**

Rapid Tranquilisation: not Recommended Medications

- **Intramuscular or oral chlorpromazine**
 - ✓ a local irritant if given IM;
 - ✓ is erratically absorbed;
 - ✓ causes hypotension (α -adrenergic receptor block) especially in the doses required for rapid tranquillisation;
 - ✓ may prolong its effect on QTc intervals
- **Intramuscular diazepam: slowly adsorbed**

Parenteral Benzodiazepines for Acute Agitation (↑↑ GABA-ergic transmission)



Initial
Onset (min)^a Dose^b (mg) Considerations

<i>Benzodiazepines</i>			
Diazepam	30	5–10 IV	Avoid IM because of unpredictable absorption. Useful in the setting of alcohol withdrawal
Lorazepam	2–5 IV 15–30 IM	1–2 IM/IV	—
Midazolam	3 IV 4–6 h IM	2.5–5	Higher risk of respiratory depression compared with lorazepam and diazepam
Delorazepam	?	2-5 IM/IV	T max IM: 40 min T ½.: 130,8 (±28,5) hours

IPNOVEL (MIDAZOLAM)

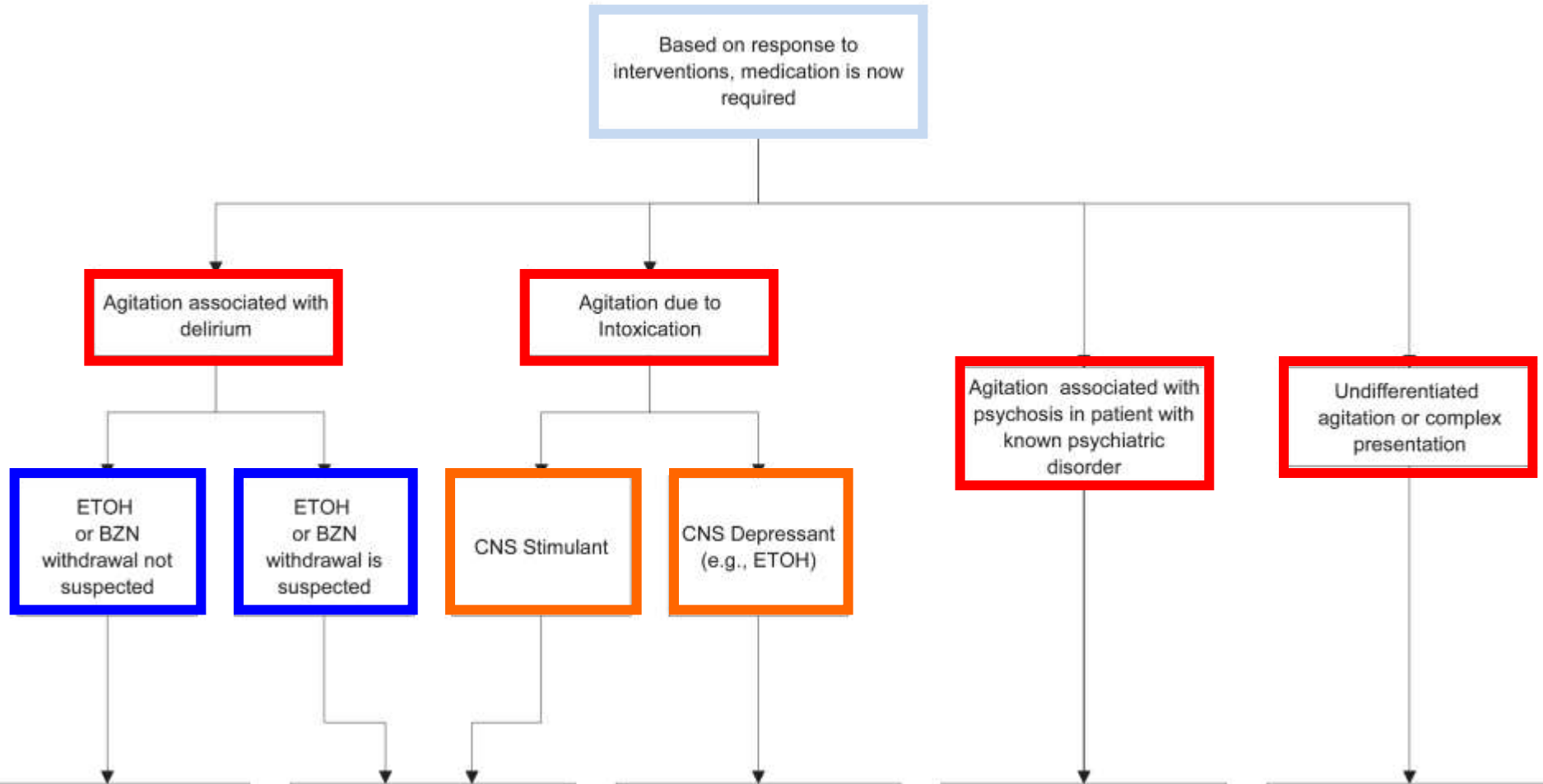
Indicazioni Terapeutiche - Scheda Tecnica

- **Ipnovel è un farmaco ipno-inducente a breve durata d'azione**
- **Indicato in:**
 - **sedazione conscia prima e durante procedure diagnostiche o terapeutiche con o senza anestesia locale.**
 - **anestesia: premedicazione prima dell'induzione dell'anestesia;**
 - **induzione dell'anestesia; come componente sedativo nell'anestesia combinata.**
 - **sedazione in terapia intensiva**



*Off label
come
ansiolitico*

BETA - Protocol for Treatment of Agitation (I)



BETA - P

Identify and correct any underlying medical conditions

of Agitation (II)

Avoid BZN

1. Oral 2nd-generation Antipsychotics

risperidone 2 mg
olanzapine 5-10 mg

2. Oral 1st-generation Antipsychotics

haloperidol (low dose) #

3. Parenteral 2nd-generation Antipsychotics

olanzapine 10 mg IM
ziprasidone 10-20 mg IM

4. Parenteral 1st-generation Antipsychotics

haloperidol (low dose) # IM or IV (with caution) †

There is strong evidence that doses above 3 mg (per day) in patients with delirium are associated with significant risk of EPS,⁴⁶ so patients receiving > 3mg/day should be assessed carefully for EPS.

Agitation



ETOH
or BZN
withdrawal not
suspected

BETA - Protocol for Treatment of Agitation (VI)

Agitation associated with psychosis in patient with known psychiatric disorder

1. Oral 2nd-generation Antipsychotics

risperidone 2 mg[‡]
olanzapine 5-10 mg[‡]

2. Oral 1st-generation Antipsychotics

haloperidol 2-10 mg with BZN

3. Parenteral 2nd-generation Antipsychotics

olanzapine 10 mg IM[‡]
ziprasidone 10-20 mg IM[‡]
aripiprazole 9,75 mg IM

4. Parenteral 1st-generation Antipsychotics

haloperidol 2-10 mg IM with BZN

‡ If an antipsychotic alone does not work sufficiently, add lorazepam 1-2 mg (oral or parenteral).

BETA - Protocol for Treatment

1. Oral Benzodiazepines

lorazepam 1-2 mg

chlordiazepoxide 50 mg

diazepam 5-10 mg

2. Parenteral

Benzodiazepines

lorazepam 1-2 mg IM or IV

Undifferentiated
agitation or complex
presentation

No Psychosis Evident

Same as agitation due to
withdrawal

Psychosis Evident

Same as for primary
psychiatric disorder

NICE Guidelines on Drugs Used for Rapid Tranquilisation

Benzodiazepines

- First line treatments in a non psychotic context
- Lorazepam often chosen as the first drug of choice in rapid tranquillisation
 - shorter elimination half-life than many other BZDs, which limits the risk of excessive sedation due to the cumulative effects of the drug.

Antipsychotics*

- Commonly used as second line treatments
- Also used in some cases as first line treatments if benzodiazepines are contraindicated or have proven ineffective in the past

Combination of BZD + antipsychotic

- To achieve early onset of calming/sedation,
- Or to achieve a lower dose of antipsychotic in the context of psychosis, an oral antipsychotic in combination with oral lorazepam, should be considered in the first instance.

- No evidence of a higher incidence of adverse effects with this combination

***Atypical antipsychotics, with or without benzodiazepines, should be considered first in the treatment of acute agitation².**

NICE Guidelines: Rapid Tranquilisation (II)

- If immediate tranquillisation is essential then **intravenous administration** may be necessary.
- **IV administration of BDZs or haloperidol** should not normally be used except in very exceptional circumstances, which should be specified and recorded.
- In very exceptional circumstances, which should be specified and recorded, **IM haloperidol in combination with IM promethazine, or IM midazolam alone** may be considered as an alternative to IV administration of benzodiazepines or haloperidol.

La Cassetta degli Attrezzi

	Orale	IM	EV
<i>Benzodiazepine</i>	lorazepam delorazepam	lorazepam	lorazepam midazolam* delorazepam
<i>AP Tradizionali</i>	aloperidolo [°]	aloperidolo [°] promazina	aloperidolo [°]
<i>AP II Generazione</i>	olanzapina orodispersibile risperidone soluzione	aripiprazolo	
<i>Altri</i>		prometazina (antistaminico)	

*off-label; °warning

Per una Pratica Migliore

- **Tratta l'eventuale causa medica sottostante**
- **Somministrazione orale quale prima via**
- **Considera le preferenze del paziente**
- **Inizia con il dosaggio più basso possibile**
- **Non associare più composti nella stessa siringa**
- **Non associare più farmaci della stessa classe**
- **Aggiornati sulle norme regolatorie**
- **Motiva dettagliatamente le scelte off-label**