South London and Maudsley NHS

Psychosis Clinical Academic Group (CAG)

LEARNING FROM END-STAGE RAPID TRANQUILLISATION IN WOMEN'S PICU

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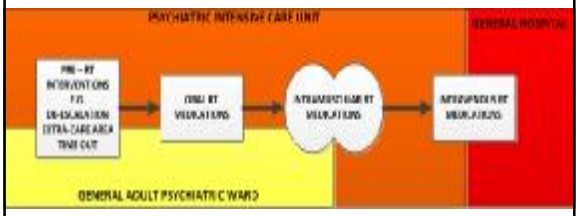
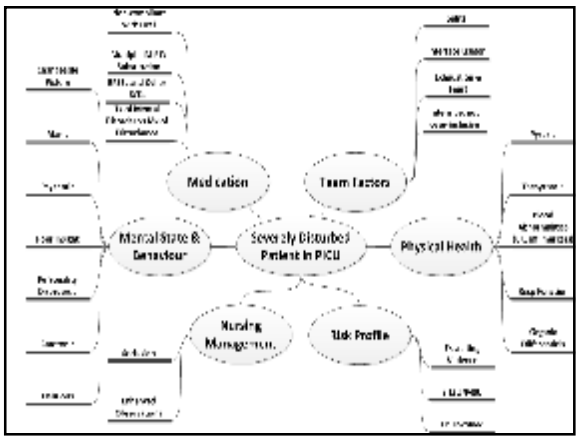
## RAPID TRANQUILLISATION




## Intramuscular Medication - Benzodiazepines

- LORAZEPAM
- 0.5-2mg IM every 1-2 hours until symptoms controlled
- Cmax: PO 1-6hrs; IM 45-75min; IV 5-10min
- Onset of efficacy: 5-30min
- Elim half-life: 8-24hrs
- Metabolites: not active
- No accumulation with repeated doses (unlike Diazepam)

## Intramuscular Medication - Benzodiazepines

- Midazolam (unlicensed)
- Cmax: 1 min
- Effective in 5-20min
- Elim half-life: 1-4hrs(p); 1-20hrs(m)
- Metabolites: active

- Diazepam
- Cmax: 1-2hrs
- Not much faster than oral in terms of efficacy
- Elim half-life: 15-80hrs(p); 30-200hrs(m)
- Metabolites: active
- IM erratically absorbed
- Accumulation in chronic dosing

## Intramuscular Medication - Antipsychotics

- Olanzapine
- 10mg at least as effective as 7.5mg Haloperidol
- Peak in a few minutes
- Peak plasma 5x higher than oral dosing
- Onset of efficacy in 30min
- Max combined dose 20mg/day
- Max IMs in 24hrs is three
- Short-term only: max for 3 consecutive days
- No simultaneous benzos (2hrs apart)

## Intramuscular Medication - Antipsychotics

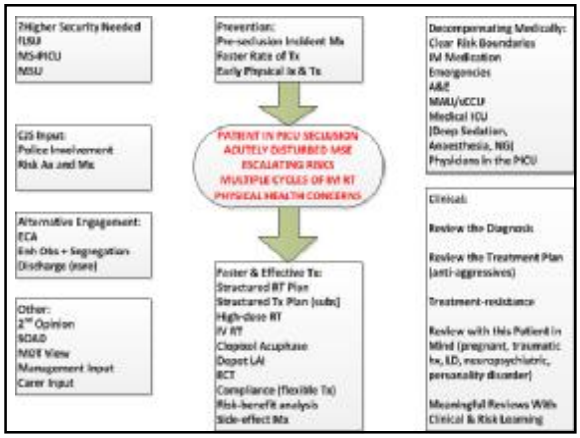
- Haloperidol
- Usually 30-60min till sedation achieved
- Max 18mg per day (IM)
- Current concerns:
- Reilly et al (Lancet 2000)
- QTc Prolongation
- Torsades de pointes
- SPC: Cardiac Ax & ECG
- Akathisia

## Intramuscular Medication - Antipsychotics

- Aripiprazole
- Onset of efficacy 30-60min
- Usual dose 5.25-9.75mg.
- IMs at least 2hrs apart.
- Max doses in 24hrs is three.
- Max combined dose in 24hrs is 30mg.
- Benzos can be given at the same time.
- Specific anti-agitation effect vs non-specific sedative effect.

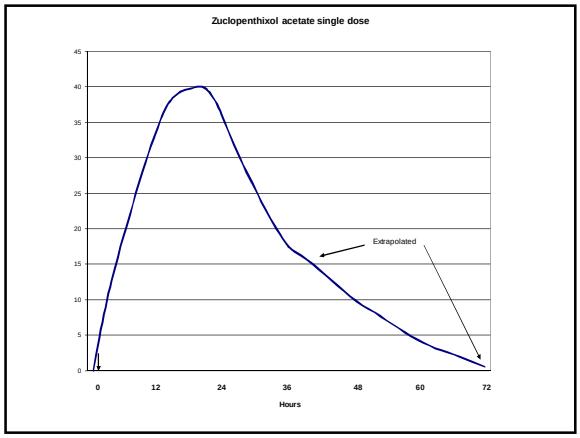
## RT Medication - Other

- Promethazine (PO/IM)
- IM Combinations: Antipsychotic + Benzodiazepine
- IM Combinations: Haloperidol + Promethazine
- IM Chlorpromazine X
- IM Amylobarbitone Sodium 500mg X
- IM Paraldehyde X
- IM Zuclopenthixol Acetate (?)
- IV Medn: Diazepam (?Haloperidol) (?Midazolam)




## Acuphase

- Cmax: On average 24-36 hours post-IM
- Sedation begins in 2hrs, but peaks after 12hrs
- Effects can last up to 24hrs
- 50-150mg; max 400mg in a 2-week period (and max 4 injections in that time)
- Injections <u>at least</u> 24hrs apart
- This is clearly not RT!!!
- BNF states you can go to LAI with last injection of Acuphase!



## ECT – Do We Use It Enough?

- RCPsych Consensus Group (2003): Major Depression; Mania; Acute Schizophrenia; Catatonia.
- NICE (2005): Severe Depressive Illness; Catatonia; Prolonged or Severe Manic Episode (not in the mx of schizophrenia!)
- RCPsych ECT Handbook (2004): Severe mania that has not responded to treatment of choice; Catatonia when Lorazepam has been ineffective

## Anti-Aggressives

- Lithium (PO)
- Risperidone (LAI) / Clozapine / Quetiapine / Zuclopenthixol (SAI and LAI)
- Benzodiazepines (for short-term) (IM)
- Valproate (loading – PO)

Hyperthermia Syndromes In Psychiatry
Ahuja N & Cole A. Advances In Psychiatric Treatment (2009)

| DIFFERENTIAL DIAGNOSES |
|---|
| Neuroleptic Malignant Syndrome |
| Serotonin Syndrome |
| Malignant (Lethal) Catatonia |
| Anticholinergic Toxicity Syndrome |
| Exertional Heat Stroke |
| Sepsis |
| Encephalitis, Meningitis |
| Thyrotoxicosis |
| Overdose of Sympathomimetics and Other Drugs |
| Alcohol or Drug Withdrawal Delirium |

## RT/ Sedation/ Anaesthesia

- RT (Urgent Sedation): reduction in agitation and aggression via light sedation, allowing a thorough psychiatric assessment
- Deep Sedation: reduction of consciousness and motor and sensory activity, verbal contact is progressively lost
- Anaesthesia: unconsciousness, analgesia and muscle relaxation. Loss or airway control and protective reflexes.

## Sedative Agents In The ICU

- Drug Classes:
- Opioids: Fentanyl; Remifentanil; Morphine Sulphate
- Benzos: Diazepam; Lorazepam; Midazolam
- Other: Dexmedetomidine; Propofol; Clonidine; Ketamine
- Aims of sedation/analgesia: facilitate intubation/ventilation; provide relief from anxiety/pain; decrease O2 requirements

## Psychiatric Medications and Nasogastric Tubes


BMJ Case Reports

Novel treatment (new drug/intervention; established drug/procedure in new situation)

Successful treatment of acute mania and perineal abscess using dexmedetomidine sedation as adjunctive therapy

Adam L. Ackerman,[1] Cristin Mount[2]

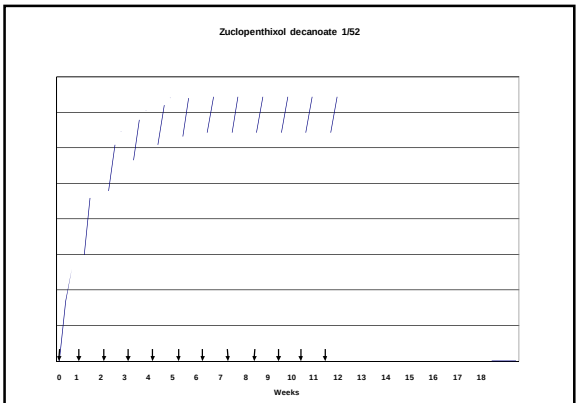

CLINICAL AND RESEARCH REPORTS

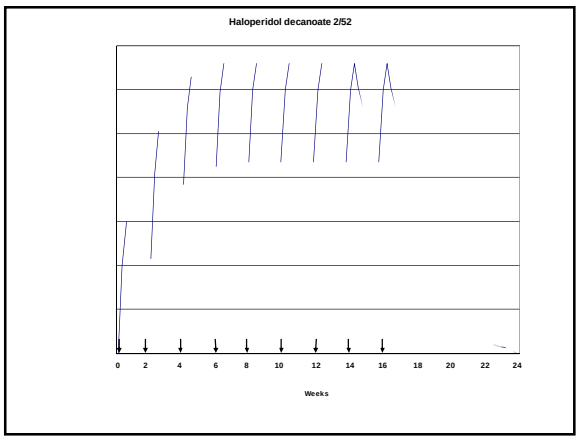
Adjunctive Valproic Acid for Delirium and/or Agitation on a Consultation-Liaison Service: A Report of Six Cases

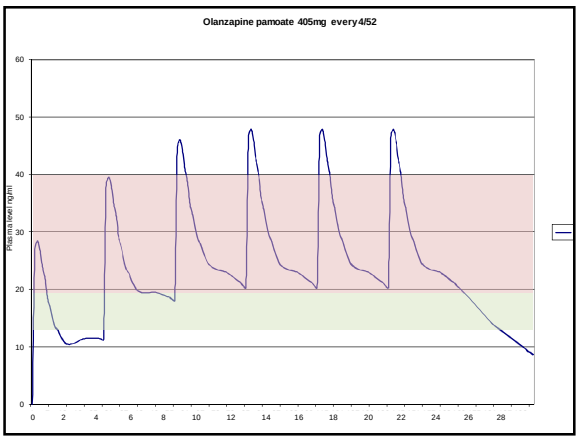
James A. Bourgeois, O.D., M.D.
Alan K. Kolko, M.D., M.S.H.S.
Jamie E. Simmons, M.D.
Sarah Tellos, M.D.
Christopher Eggleston, J.D., M.D.

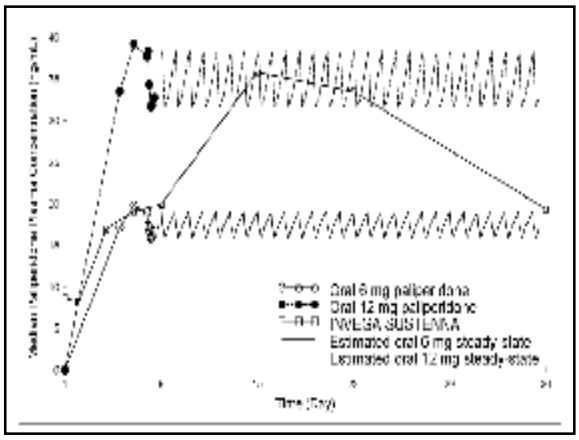
## LAIs

| | |
|---|---|
| Flupenthixol Decanoate | Oil |
| Fluphenazine Decanoate | Oil |
| Haldol Decanoate | Oil |
| Pipothiazine Decanoate | Oil |
| Zuclopenthixol Decanoate | Oil |
| Risperdal Consta | Biodegradable Microspheres |
| Paliperidone Palmitate | Crystalline |
| Olanzapine Pamoate | Crystalline |




## LAIs

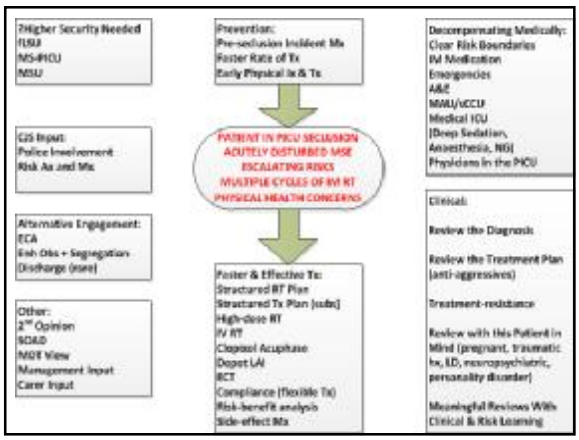
- Dose Response Relationships Are Complex
- Most LAIs reach steady-state after 4-5 half-lives (over 2 months!)
- But prior to steady-state, plasma profile can vary several-fold
- Loading (initiation) strategies allow for earlier steady-state
- Is Loading/Initiation a bridge between the acute and maintenance role of the LAI?

## LAIs – Loading?

| Name | Delivery | Loading Strategy |
|---|---|---|
| Flupenthixol Decanoate | Oil | ↑ frequency<br>• e.g. HD wkly will quadruple plasma levels in the short-term<br>• Expect EPSEs and other S/Es<br>• min effective dose not clear! |
| Fluphenazine Decanoate | Oil | |
| Haldol Decanoate | Oil | |
| Pipothiazine Decanoate | Oil | |
| Zuclopenthixol Decanoate | Oil | |
| Risperdal Consta | Biodegradable Microspheres | Not possible due to low release prior to approx 24 days |
| Paliperidone Palmitate | Crystalline | Initiation strategies have been developed to increase immediate plasma levels, but SS still takes months |
| Olanzapine Pamoate | Crystalline | |

## Valproate Loading (pre-emptive)

- Antimania at levels of 45-125 µg/ml
- > 110 µg/ml: S/E > treatment benefit
- Antimanic response as early as day 5
- Keck et al 1993: 20mg/kg
- Hirschfield et al 1999: 30mg/kg (D1+2); 20mg/kg (D3-10)
- ?60 kg lady. Load with 1500mg (750BD), and check level in 3-5 days.




## In Summary

- PICU patients are all challenging
- Some more than others
- End-stage Rapid Tranquillisation scenarios are some of the most challenging in the PICU
- These cases also lead to good learning opportunities
- Innovative practice in the face of serious challenge is a core attribute of a PICU team

## My Learning:

- Pharmacokinetics and dose-response
- IM, IV and ECT Tx in ES-RT
- Knowledge of psychiatric and medical syndromes
- Keep out-of-date and up-to-date
- Look for patient-specific factors
- High quality medical liaison
- Consider the treatment setting early
- Treatment is multidisciplinary; receive and share learning with the team