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RCSI

Intravenous Paracetamol – outcomes from an audit in the Irish hospital setting

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Background

- IV paracetamol introduced to the market in 2003
- In intervening years accruing evidence of potential for harm
  - Especially among children
- Errors in dosing, frequency, MDD etc.
  - Resulting in morbidity & mortality
- Lack of adherence to appropriate licensed recommendations for its use
- In tandem a significant increase in use

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Patient Safety First

REFERENCES

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3 Gray T, Hoffman RS, Bateman DN. Intravenous paracetamol – an international perspective of toxicity. *Clin Toxicol* 2011:**29**:150–152.

4 MHRA Drug Safety Advice. Intravenous paracetamol (Perfalgan®): risk of accidental overdose, especially in infants and neonates. *Drug Safety Update* 2010;**3**(12):2–3 (accessed 4 November 2012).

5 Overdose of intravenous paracetamol in infants and children: Signal Alert 29 October 2010. *NPSA* (accessed 4 November 2012).

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7 Berling I, Anscombe M, Isbister GK. Intravenous paracetamol toxicity in a malnourished child. *Clin Toxicol* 2012;**50**:74–76.

8 Savino F, Maddalena ML, Locatelli E et al. Fulminant hepatitis after 10 days of acetaminophen treatment at recommended dosage in an infant. *Pediatrics* 2011;127:e494-e497.

9 Dart RC, Rumack BH. Intravenous acetominophen in the United States: iatrogenic dosing errors. *Pediatrics* 2012;**129**:901–902.

IMSN recommendations on how to reduce risk (2012)

- ✓ Restrict use (only if po / pr routes not appropriate)
- ✓ Dose by body weight (50kg & under)
- ✓ Check last dose
- ✓ Patients at risk of toxicity
- ✓ Use 50mL presentation for smaller patients
- ✓ Mixing
- ✓ Education

A number of single site audits undertaken in Irish hospitals

Aim of audit

- To determine the adherence to best-practice recommendations for use of IV paracetamol in a selection of Irish hospitals

- Research question:
  - Is IV paracetamol prescribed and administered according to best practice guidelines in a sample of Irish hospitals?

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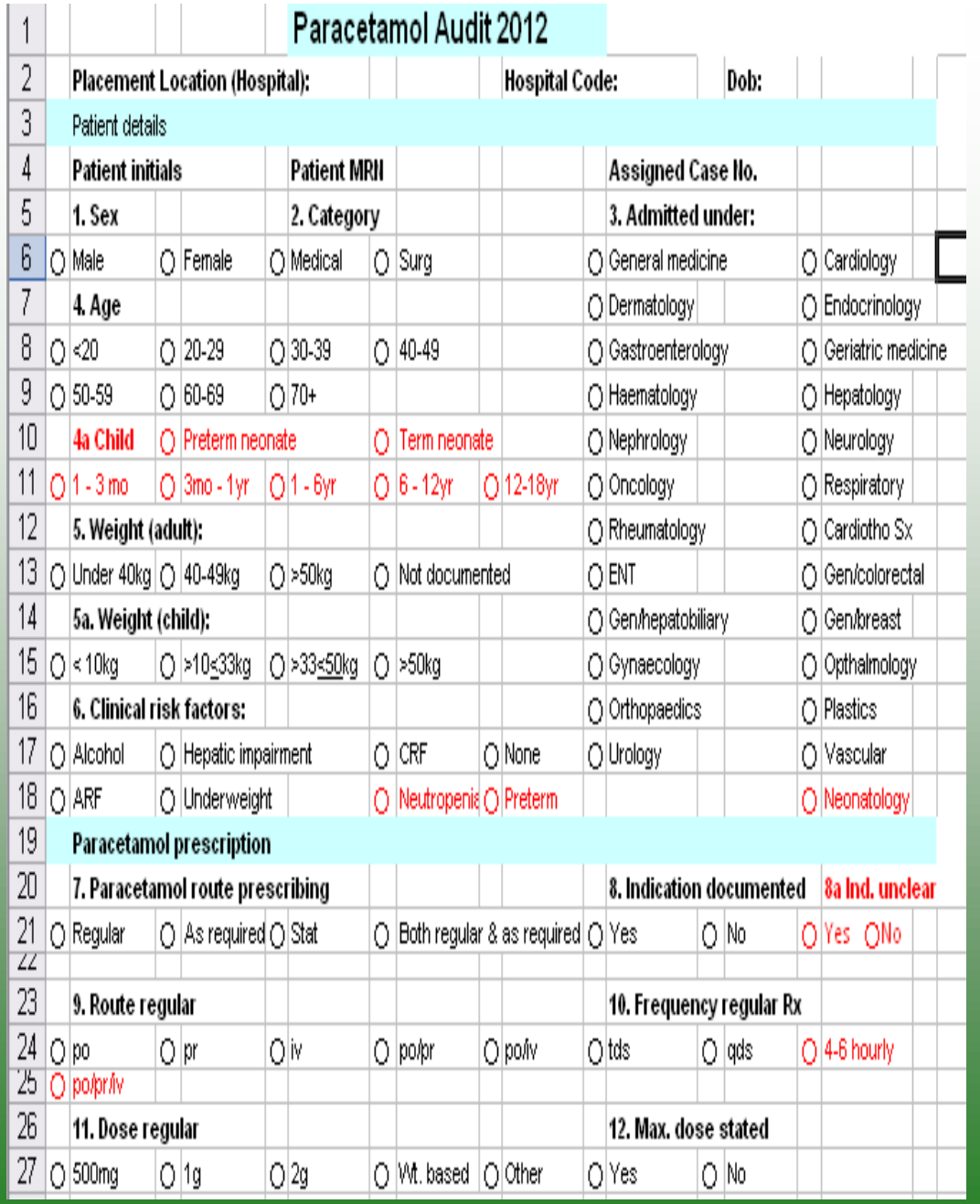
Methods

- MPharm NPIP programme - RCSI
- 5 participating hospitals
  - 3 adult
  - 1 paediatric
  - 1 mixed
- Practical resources
  - Protocol development
  - Data collection form
  - Codebook
  - Database
- Collaborative approach

Existing in-house guidelines



Paracetamol Audit 2012

Placement Location (Hospital): **Hospital Code:** **Dob:**

Patient details

Patient initials **Patient MRII** **Assigned Case No.**

1. Sex **2. Category** **3. Admitted under:**

○ Male	○ Female	○ Medical	○ Surg			○ General medicine		○ Cardiology	
4. Age						○ Dermatology		○ Endocrinology	
○ <20	○ 20-29	○ 30-39	○ 40-49			○ Gastroenterology		○ Geriatric medicine	
○ 50-59	○ 60-69	○ 70+				○ Haematology		○ Hepatology	
4a Child	○ Preterm neonate		○ Term neonate			○ Nephrology		○ Neurology	
○ 1 - 3 mo	○ 3mo - 1yr	○ 1 - 6yr	○ 6 - 12yr	○ 12-18yr		○ Oncology		○ Respiratory	
5. Weight (adult):						○ Rheumatology		○ Cardiotho Sx	
○ Under 40kg	○ 40-49kg	○ >50kg	○ Not documented			○ ENT		○ Gen/colorectal	
5a. Weight (child):						○ Gen/hepatobiliary		○ Gen/breast	
○ < 10kg	○ >10≤33kg	○ >33≤50kg	○ >50kg			○ Gynaecology		○ Opthalmology	
6. Clinical risk factors:						○ Orthopaedics		○ Plastics	
○ Alcohol	○ Hepatic impairment		○ CRF	○ None		○ Urology		○ Vascular	
○ ARF	○ Underweight		○ Neutropenic	○ Preterm				○ Neonatology	

Paracetamol prescription

7. Paracetamol route prescribing						**8. Indication documented**		**8a Ind. unclear**	
○ Regular	○ As required	○ Stat	○ Both regular & as required			○ Yes	○ No	○ Yes	○ No
9. Route regular						**10. Frequency regular Rx**			
○ po	○ pr	○ iv	○ po/pr	○ po/iv		○ tds	○ qds	○ 4-6 hourly	
○ po/pr/iv									
11. Dose regular						**12. Max. dose stated**			
○ 500mg	○ 1g	○ 2g	○ Wt. based	○ Other		○ Yes	○ No		

Development of protocol

- Study design
- Data collection methodology
- Exclusion/inclusion criteria
- Definition of risk factors key
  - Weight
  - Renal insufficiency
  - Alcohol risk*
  - Hepatocellular insufficiency*

Audit demographics

- IV paracetamol primary focus in 4 hospitals
  - All paracetamol prescriptions in 1
  - Of necessity all paracetamol prescriptions reviewed
- Duration of data collection: 4 - 14 days
- Both medical & surgical in 4 hospitals
- Intern data collection in 4/5

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Patient characteristics

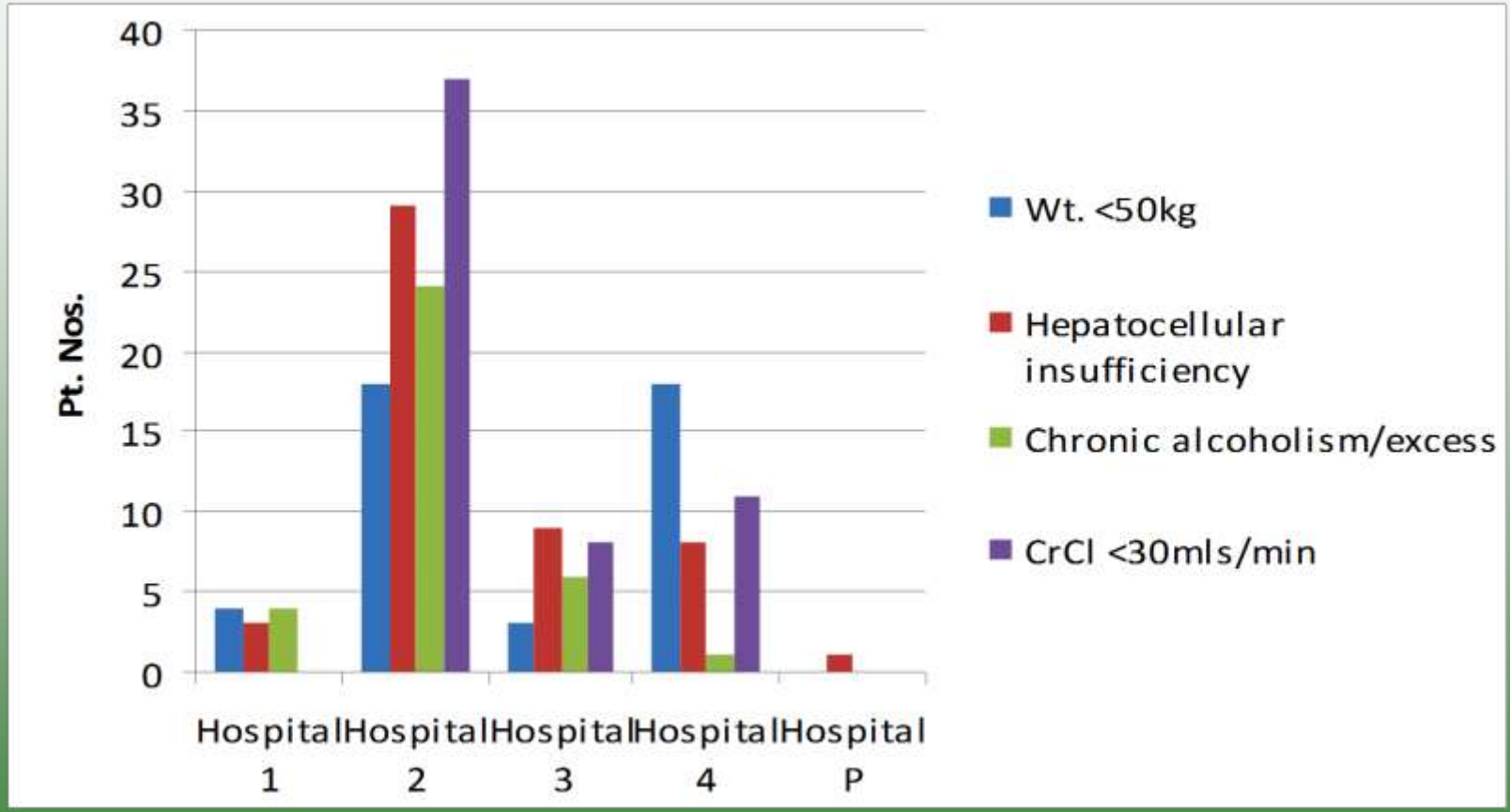
	Pt. Nos.	Medical pt.	Male gender	Age Mean/median (range/SD)	Wt. (kg)** Range
Hospital 1	50	0%	62%	54 (20-83)	N=44 >50kg
Hospital 2	274	54%	51%	64 (2-95)	N=111 >50kg
Hospital 3	101	38%	55%	Med 64 (17-93)	73 (46-139)
Hospital 4	43	81%	23%	Med 77 (+/- 16)	52 (35-86)
Hospital P	131	65%	53%	Med 5 (1-20y)	1.1-82.6

**** For those whose weight was available**

Proportion of patients for whom weights available

- Ranged from 46% to 98%
- Paediatric hospital highest compliance
- Significant absence of weights accessible to prescribers
- Inherent impact on ability to determine appropriate dose

Prevalence of risk factors



Numbers represent those for whom risk factor was documented

Prescribing factors

- Capacity for po in 79 - 97% of patients prescribed IV
- Prescribing in regular + prn section in all hospitals
- Prescribing by multiple routes significant
  - IV in addition to po most common
- Dose adjustments according to risk factors not routine
- Duplicate prescriptions highlighted in 1 hospital
  - N = 15 patients, clinical pharmacy endorsement / nursing intervention avoided administration in n = 3 patients
- Maximum daily dose not routinely written
  - Endorsement by clinical pharmacists

Adherence to best-practice recommendations

- Classifications:
  - –Potential to exceed maximum recommended dose in at risk patients
  - –Inappropriate dose frequency reduction in patients with renal insufficiency
  - –Continuation of IV doses exceeding 24 hours
- Results:
  - – Ranged from 37% to 81%
  - – Lowest figure associated with prevalence of unknown weight
  - – Average when low outlier removed = 78% adherence

‘Case reports’

- One patient with renal impairment received 1g IV 3h apart
- One patient with hepatic impairment received 2g IV intraoperatively & 3g po within 24 hours
- Patients with CrCl<30ml/min, one third dosed appropriately
- In patients <50kg, 33% prescribed according to guidelines
- Dosing in preterm and neonates inaccurate (low patient numbers)
- One hospital reported absence of checking when last dose of paracetamol administered

Strengths & Limitations

- Strengths
  - Large patient cohort across a broad range of hospitals
  - Degree of similarity in results
- Limitations
  - Degree of heterogeneity in terms of data collection, data collation and analysis
  - Pooled dataset unavailable
    - Univariate & bivariate analysis
  - Generalisability of the data compromised

Take home messages

- Scope to improve documentation of weight in an accessible way for prescriber
- Increased vigilance in prescribing for IV paracetamol in line with best-practice recommendations
  - Particularly for at risk patients
- Audit tools available for follow-up audit and pooling of data in original sites or other sites

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BJCP British Journal of Clinical Pharmacology

INTRAVENOUS PARACETAMOL

Safe Anaesthesia Liaison Group

SALG RECOMMENDATIONS

1. Intravenous (IV) paracetamol should be prescribed carefully, according to the weight, age and co-morbidities of the patient. The upper dose limit for each single dose and in each 24-hour period should not be exceeded.
2. 50ml vials of IV paracetamol should be used for patients less than 33kg. In infants and small children, doses should be measured accurately using a syringe.
3. Enquiry about recent paracetamol ingestion should form part of routine pre-operative assessment. All doses of paracetamol administered in the operating theatre should be recorded on the ward drug administration chart and in the anaesthetic record.
4. Advice should be sought from the local poisons information service in all cases of overdose of intravenous paracetamol. Treatment with acetylcysteine is suggested following a single dose greater than 60mg/kg.
5. Intravenous paracetamol (Perfalgan®) remains under intensive monitoring by the MHRA. All suspected adverse reactions to IV paracetamol should be reported to the Yellow Card Scheme and discussed with the local poisons information service.

Dispensing

Conclusion

- 2012 audit showed that prescribing of IV paracetamol could be improved
- A number of recommendations highlighted in each participating site
- Rolling collaborative audits would provide evidence of impact of recommendations
- Additional safety issues may exist in peri-operative setting with admixtures with other agents

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