Guideline for Oral and Intravenous Dosing of Paracetamol in ADULTS

University Hospitals of Leicester NHS
NHS Trust
Trust Reference B13/2012

1. Introduction

Paracetamol can cause liver damage in patients who are have certain identifiable risks factors and therefore therapeutic dosing may need to be reduced. Intravenous therapy is shown to have a higher peak plasma level than oral and patients with a low body weight <50kg will need a reduced dose regardless of whether risk factors are present or not. The aim of this guideline is to provide safe dosing for oral and intravenous paracetamol in ADULT patients.

2. Scope

The Guideline covers all ADULT patients treated within UHL. For dosing in children refer to the BNFC. This guideline is for use by all staff who prescribe or administer paracetamol medication in adults.

3. Oral dosing

Paracetamol has a narrow therapeutic index. Low body weight is not directly correlated with an increased risk for oral paracetamol, but low body weight may indicate other conditions which may be a risk factor for example malnutrition or anorexia.

Toxicity can occur when the patient has identifiable risk factors for liver toxicity (see section 5). There is no formal guidance for adjusting oral dosing and doses have been based on the Clinical Knowledge Summary commissioned by National Institute for Health and Care Excellence 2020. Patients who require a dosage adjustment must be advised that this is lower than the maximum dose of paracetamol recommended in package inserts.

4. Intravenous dosing

Intravenous administration of paracetamol results in higher peak plasma levels than the same dose given orally. The product license specifies that the standard maximum daily dose of 4g daily must be decreased in patients with a body weight ≤50kg or in those with risk factors for toxicity. The dosing interval needs to be increased in patients with severe renal impairment. [4]

5. Risk factors for hepatotoxicity

Risk factors include:

a) Malnourished patients, with nutritional deficiency and/or chronic debilitating illness and therefore likely to be glutathione deplete [3] Conditions, such as those listed below are likely to deplete glutathione concentrations which may result in the metabolite N- acetyl-p-benzoquinone imine (NAPQI) accumulating and exerting a direct hepatotoxic effect
e.g.
- acute (patients not eating for a few days) or chronic starvation,
- eating disorders (anorexia or bulimia),
- cystic fibrosis,
- AIDS,
- cachexia,
- alcoholism,
- Hepatitis C.

b) Hepatic enzyme induction or evidence of on-going liver injury e.g. long term treatment with liver enzyme-inducing drugs such as carbamazepine, phenobarbital, phenytoin, primidone,

rifampicin, rifabutin, efavirenz, nevirapine, St John's Wort;

c) regular consumption of ethanol in excess of recommended amounts, particularly if nutritionally compromised.

DOSE ADJUSTMENT OF PARACETAMOL IN ADULTS

(see separate guidance in children)

1. Record patient weight on drug chart. – paper or emeds
2. Assess the patient for risk factors for toxicity.
3. If risk factors are present REDUCE the total daily dose.
4. Prescribe the oral dose in multiples of 500mg of paracetamol.
5. Do not exceed four doses of paracetamol in 24 hours.
6. Details on IV administration can be found in the IV guide

Dose of ORAL paracetamol in ADULT patients WITHOUT risk factors
500mg-1g every 4-6 hours **Maximum 4g daily** Consider dose reduction in patients with very low body weight

Recommended dose adjustments of ORAL paracetamol in ADULT patients WITH risk factors	
30- 39kg	**15mg/kg four times a day. Maximum 60mg/kg in 24 hours**
40- ≤ 50kg	**1g TDS or 15mg/kg every 4-6 hours** **Maximum 3g daily**
> 50kg	**500mg-1g every 4-6 hours** **Maximum 4g daily**

Dose of IV paracetamol in ADULTS	
≤ 33kg with or without risk factors	**15mg/kg per dose every 4-6 hours** **Maximum 2g daily**
>33 - ≤ 50kg with or without risk factors	**15mg/kg per dose every 4-6 hours** **Maximum 3g daily**
> 50kg with risk factors	**500mg - 750mg every 4-6 hours** **Maximum 3g daily**
> 50kg with no risk factors	**1g every 4-6 hours** **Maximum 4g daily**
Renal function GFR<30ml/min	**Dose according to weight and risk factors but increase the minimum dosing interval to 6 hours**

6. Monitoring and Audit Criteria

6.1 Key performance indicators / audit standards

Key Performance Indicator	Method of Assessment	Evidence
Dose reduction of oral paracetamol in adults with risk factors	Monthly monitoring of Datix incident reports. 1 year pharmacy audit with subsequent audits depending on results and Datix reports if necessary	Monthly Datix report Audit results
Dose reduction of oral paracetamol in adult patients with body weight <50kg but no risk factors	Monthly monitoring of Datix incident reports. 1 year pharmacy audit with subsequent audits depending on results and Datix reports if necessary	Monthly Datix report Audit results
Dose reduction of IV paracetamol in adult patients <50kg	Monthly monitoring of Datix incident reports. 1 year pharmacy audit with subsequent audits depending on results and Datix reports if necessary	Monthly Datix report Audit results

6.2 Reporting and Escalation

Monthly Datix report will be reviewed Medication Safety Lead Pharmacist and any concerns regarding the prescribing of paracetamol and repeat issues will be emailed to the CMG Quality and Safety Lead for action.

Pharmacy audits and reports – results are reported to UHL Medicines Optimisation Committee and any concerns regarding practice will be actioned through this committee.

Medication Safety Lead is responsible for reporting results and escalating concerns to the Medicines Optimisation Committee.

This policy will be included within medicines management induction training

7. Further information / References

1. Management of Paracetamol Poisoning Therapeutic Excess. Toxbase online at www.toxbase.org/
2. Lee Claridge et al. Acute liver failure after administration of paracetamol at the maximum recommended daily dose in adults. British Medical Journal 2010: 341; 1269-1270
3. BNF http://www.medicinescomplete.com/mc/bnf/current/PHP188-analgesics-non-opioid.htm#PHP191
4. Summary of Product Characteristics Perfalgan 10mg/ml solution for infusion.

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT

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REVIEW RECORD

Date	Issue Number	Reviewed By	Description Of Changes (If Any)
12/4/2019	3	Medoc	None made
19/7/2019	3	PGC	None made
7/3/2023	4	PGC	Consider dose reduction for oral in low body weight pts in response to the HSIB report

DISTRIBUTION RECORD:
