

Table 1

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Hulbert, 1991, UK ¹	30 patients with corneal abrasion after foreign body removal Chloramphenicol and eye patch <i>v</i> chloramphenicol alone	PRCT	Discomfort Time to healing	Greater at 24 hours No difference	
Kirkpatrick <i>et al</i> , 1994, UK ²	Patients with simple traumatic corneal abrasions Antibiotic, mydriatic, and eye patch <i>v</i> antibiotic and mydriatic alone	PRCT	Time to healing	Significantly (<0.05) better in antibiotic alone group	
Patterson <i>et al</i> , 1996, USA ³	33 patients with eye pain and corneal abrasion Eye patch <i>v</i> no eye patch	PRCT	Pain score Analgesic use	No difference No difference	Small study, low power
Kaiser, 1997, USA ⁴	201 patients with non-infected non-contact lens related traumatic (120) or after foreign body removal (81) corneal abrasions Antibiotic, mydriatic, and eye patch <i>v</i> antibiotic and mydriatic alone	PRCT	Pain Time to healing Blurred vision	Significantly less in antibiotic/mydriatic alone group Significantly less in antibiotic/mydriatic alone group Significantly less in antibiotic/mydriatic alone group for traumatic abrasions, no difference for abrasions after foreign body removal	
Campanile <i>et al</i> , 1997, USA	64 patients with traumatic corneal abrasion Patched <i>v</i> unpatched	PRCT	Rate of healing at day 1	Significantly faster in unpatched	Only recorded at 1 day
Arbour <i>et al</i> , 1997, Canada	48 eyes (46 patients) with corneal erosion Patching <i>v</i> no patching	PRCT	Linear and surface speed of re-epithelialisation Pain Insomnia	No significant difference No significant difference No significant difference	

PRCT = prospective randomised controlled trial.

Paracetamol or ibuprofen in febrile children

Report by Simon Carley, *Clinical Fellow*
Search checked by Martin Thomas, *Research Fellow*

Clinical scenario

A 3 year old girl presents to the emergency department after a convulsion. She has a three day history of sore throat, cough, and fever. She has had two previous febrile convulsions. She is still hot and irritable. You wish to reduce the temperature, provide symptomatic improvement, and wonder whether Calpol (paracetamol syrup) or Junifen (ibuprofen syrup) would be more effective.

Three part question

[In children with a significant fever] is [paracetamol better than ibuprofen] at [reducing fever and reducing fever induced irritability]?

Search strategy

Medline 1966 to 12/98 using the OVID interface. {[exp acetaminophen OR acetaminophen.mp OR paracetamol.mp] AND [child.mp OR children\$.mp] AND [exp anti-inflammatory agents, non-steroidal OR non-steroidal anti-inflammatory agents.mp OR exp ibuprofen OR ibuprofen.mp] AND [exp fever

OR fever\$.mp OR febrile.mp] AND [maximally sensitive RCT filter]} LIMIT to human AND english language.

Search outcome

Fifty five papers were found of which 33 were irrelevant and seven of insufficient quality for inclusion; the remaining papers are shown in table 2.

Comment

While a number of well designed studies show ibuprofen to be more effective than paracetamol at reducing temperature in febrile children, a number of others show no difference in effect. Some of the studies do not follow up the subjects for the length of time between treatment doses, their findings must therefore be interpreted with caution. A formal meta-analysis of these studies would be of value.

Clinical bottom line

Both paracetamol and ibuprofen are effective antipyretics in children. Ibuprofen would appear to cause the most rapid and prolonged reduction in temperature.

1 Amdekar YK, Desai RZ. Antipyretic activity of ibuprofen and paracetamol in children with pyrexia. *Br J Clin Pract* 1985;39:140-3.

2 Walson PD, Galletta G, Bradem NJ, *et al*. Ibuprofen, acetaminophen, and placebo treatment of febrile children. *Clin Pharmacol Ther* 1989;46:9-17.

- 3 Joshi YM, Sovani VB, Joshi VV, *et al.* Comparative evaluation of the antipyretic efficacy of ibuprofen and paracetamol. *Indian Pediatr* 1990;27:803-6.
- 4 Sidler J, Frey B, Baerlocher K. A double-blind comparison of ibuprofen and paracetamol in juvenile pyrexia. *Br J Clin Pract* 1990;70:22-5.
- 5 Wilson JT, Brown RD, Kearns GL, *et al.* Single-dose, placebo-controlled comparative study of ibuprofen and acetaminophen antipyresis in children. *J Pediatr* 1991;119:803-11.
- 6 Walson PD, Galletta G, Chomilo F, *et al.* Comparisons of multidose ibuprofen and acetaminophen therapy in febrile children. *Am J Dis Child* 1992;146:626-32.
- 7 Kauffman RE, Sawyer LA, Scheinbaum ML. Antipyretic efficacy of ibuprofen vs acetaminophen. *Am J Dis Child* 1992;146:622-5.
- 8 Kelley MT, Walson PD, Edge JH, *et al.* Pharmacokinetics and pharmacodynamics of ibuprofen isomers and acetaminophen in febrile children. *Clin Pharmacol Ther* 1992;52:181-9.
- 9 Autret E, Breart G, Jonville AP, *et al.* Comparative efficacy and tolerance of ibuprofen syrup and acetaminophen syrup in children with pyrexia associated with infectious diseases and treated with antibiotics. *Eur J Clin Pharmacol* 1994;46:197-201.
- 10 Khubchandani RP, Ghatikar KN, Keny S, *et al.* Choice of antipyretics in children. *J Assoc Physicians India* 1995;43:614-16.
- 11 Van Esch A, Van Steensel-Moll HA, Steyerberg EW, *et al.* Antipyretic efficacy of ibuprofen and acetaminophen in children with febrile seizures. *Arch Pediatr Adolesc Med* 1995;149:632-7.
- 12 McIntyre J, Hull D. Comparing efficacy and tolerability of ibuprofen and paracetamol in fever. *Arch Dis Child* 1996;74:164-7.
- 13 Autret E, Reboul-Marty J, Henry-Launois B, *et al.* Evaluation of ibuprofen versus aspirin and paracetamol on efficacy and comfort in children. *Eur J Clin Pharmacol* 1997;51:367-71.
- 14 Aksoylar S, Aksit S, Caglayan S, *et al.* Evaluation of sponging and antipyretic medication to reduce body temperature in febrile children. *Acta Paediatr Jpn* 1997;39:215-17.
- 15 Vauzelle-Kerroendan F, d'Athis P, Pariente-Khayat A, *et al.* Equivalent antipyretic activity of ibuprofen and paracetamol in febrile children. *J Pediatr* 1997;131:683-7.

Table 2

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Amdekar and Desai, 1985, India ¹	26 children with fever	PRCT	Rate of temperature reduction	No significant difference	Small numbers
	Ibuprofen 7 mg/kg <i>v</i> paracetamol 8 mg/kg		Extent of temperature reduction	No significant difference	Unblinded
Walson <i>et al</i> , 1989, USA ²	127 children aged 2-11 years with fever	Double blind PRCT	Change in temperature over 8 hours	Highest dose of ibuprofen more effective than paracetamol at speed and duration of temperature reduction	
	Ibuprofen 5 mg/kg <i>v</i> ibuprofen 10 mg/kg <i>v</i> paracetamol 10 mg/kg <i>v</i> placebo				
Joshi <i>et al</i> , 1990, India ³	175 children aged 4 months-4 years	PRCT	Change in temperature over 2 hours	Paracetamol marginally better at 30 minutes, no difference at other times	Trial only lasted 2 hours which is less than the time between doses
	Placebo <i>v</i> paracetamol 8 mg/kg <i>v</i> ibuprofen 7 mg/kg				
Sidler <i>et al</i> , 1990, Switzerland ⁴	89 children less than 14 years with fever	Double blind PRCT	Change in temperature at 3 hours	Significantly greater in the ibuprofen groups	18 withdrawals—mainly from the paracetamol group
	Ibuprofen 7 mg/kg <i>v</i> ibuprofen 10 mg/kg <i>v</i> paracetamol 10 mg/kg				
Wilson <i>et al</i> , 1991, USA ⁵	178 children aged 3 months-12 years	PRCT	Change in temperature	Greater with ibuprofen	
Walson <i>et al</i> , 1992, USA ⁶	64 children aged 6 months-11 years	PRCT	Change in temperature	No difference between highest dose ibuprofen and paracetamol	6 children withdrawn from the study
	Ibuprofen 2.5, 5, or 10 mg/kg <i>v</i> paracetamol 15 mg/kg				Small numbers in each group
Kauffman <i>et al</i> , 1992, USA ⁷	37 children with acute febrile illness	Double blind PRCT	Change in temperature at 30 min and then hourly for 8 hours	Ibuprofen and paracetamol better than placebo, higher dose ibuprofen (10mg/kg) produced a greater fall and duration of temperature loss than paracetamol	Small numbers of patients in each group
	Placebo <i>v</i> paracetamol 10 mg/kg <i>v</i> ibuprofen 7.5-10 mg/kg				
Kelley <i>et al</i> , 1992, USA ⁸	39 children aged 11 months-11 years	Double blind PRCT	Time to maximum serum concentration of drug	Longer with ibuprofen	
	Ibuprofen 6 mg/kg <i>v</i> paracetamol 10-15 mg/kg		Duration of temperature reduction	Longer with ibuprofen	
Autret <i>et al</i> , 1994, France ⁹	Children aged 6 months-5 years	Double blind PRCT	Percentage temperature reduction	Better with ibuprofen	Other clinical markers of effect (for example irritability) were not measured)
	Ibuprofen 7.5 mg/kg <i>v</i> paracetamol 10 mg/kg				

Table 2 continued

Author, date, and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Khubchandani <i>et al</i> , 1995, India ¹⁰	87 children aged 1–7 years with fever	PRCT	Change in temperature	No significant difference between ibuprofen and paracetamol	Unblinded
	Ibuprofen 7 mg/kg <i>v</i> paracetamol 10 mg/kg <i>v</i> mefenamic acid 6.5 mg/kg		Rate of fall in temperature	No significant difference between ibuprofen and paracetamol	
Van Esch <i>et al</i> , 1995, Holland ¹¹	70 outpatients with fever after febrile convulsions	Double blind PRCT	Temperature 4 hours after dose	Lower with ibuprofen (p<0.05)	The trial may be too small to show a clinically significant difference in all parameters measured
	Ibuprofen 5 mg/kg <i>v</i> acetaminophen 10 mg/kg for 3 days		Mean temperature during treatment Highest temperature during treatment	Lower with ibuprofen (p<0.05) Less with ibuprofen (p<0.05)	
McIntyre and Hull, 1996, UK ¹²	Children on paediatric wards aged 2 months–12 years	Double blind PRCT	Change in temperature	No significant difference	
	Ibuprofen 20 mg/kg/24 hours <i>v</i> paracetamol 50 mg/kg/24 hours		Irritability Clinical condition	No significant difference No significant difference	
Autret <i>et al</i> , 1997, France ¹³	Children aged 6–24 months	PRCT	Percentage temperature reduction	Ibuprofen better than aspirin or paracetamol	Unblinded study
	Ibuprofen 7.5 mg/kg <i>v</i> aspirin 10 mg/kg <i>v</i> paracetamol 10 mg/kg		Change in behaviour (irritability)	Ibuprofen better than aspirin or paracetamol	
Aksoylar <i>et al</i> , 1997, Japan ¹⁴	224 children aged 6 months–5 years with high rectal temperatures Sponging alone <i>v</i> sponging + aspirin <i>v</i> sponging + ibuprofen <i>v</i> sponging + paracetamol	PRCT	Change in temperature	Addition of antipyretic better than sponging alone Aspirin and ibuprofen better than paracetamol at reducing fever after 3 hours p>0.05	23 patients lost to follow up
Vauzelle-Kerroendan <i>et al</i> , 1997, France ¹⁵	116 children less than 12 years. Children with febrile convulsion excluded	Multicentre double blind PRCT	Time to lowest temperature	No significant difference	Rectal temperature measured by parents
	Ibuprofen 10.3 (+/- 1.9) mg/kg <i>v</i> paracetamol 9.8 (+/- 1.9) mg/kg		Extent of temperature decrease Rate of temperature decrease	No significant difference No significant difference	

PRCT = prospective randomised controlled trial.

Alkalinisation in the management of tricyclic antidepressant overdose

Report by Kevin Mackway-Jones, *Consultant*
Search checked by Martin Thomas, *Research Fellow*

Clinical scenario

A 27 year old woman presents with a history of having taken 30 tricyclic antidepressant tablets three hours before admission. Electrocardiographic monitoring shows frequent dysrhythmias. You wonder whether giving sodium bicarbonate intravenously is worthwhile.

Three part question

In a [young adult with dysrhythmias following tricyclic antidepressant overdose] is [treatment with bicarbonate better than no active treatment] at [normalising cardiovascular function]?

Search strategy

Medline 1966 to 12/98 using the OVID interface. ({[exp bicarbonates OR bicarbonate\$.mp] AND [antidepressive agents, tricyclic OR exp amitriptyline OR exp imipramine OR exp desipramine OR exp fluoxetine OR tricyclic\$.mp]} LIMIT to human AND english language).

Search outcome

Fifty four papers were found of which 43 were irrelevant and seven of insufficient quality for inclusion; the remaining papers are shown in table 3.

Comment

The evidence for current practice is all based on observational studies. The largest study recommends alkalinisation to a pH of 7.55; other studies have used fixed bicarbonate doses. There are no properly designed trials in this area.