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How genetics may impact the metabolism and elimination of celecoxib from the body and brain of children

Submission date 14/12/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 06/10/2009	**Overall study status** Completed	
Last Edited 30/08/2011	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
18/08SE

Study information

Scientific Title

The impact of genotype on plasma and cerebral spinal fluid pharmacokinetics of celecoxib in children: a randomised controlled single-centre trial

Study objectives
1. The cerebral spinal fluid (CSF) concentration of celecoxib 3 hours post oral suspension ingestion is lower than plasma levels
2. The CSF peak concentration (Cmax) of celecoxib is delayed compared to plasma Cmax
3. The CSF concentration of celecoxib is directly related to the dose ingested and underlying P450 genotype
4. Blood and CSF celecoxib concentration is directly related to age
5. Oral celecoxib dosage is directly related to quality of life and inversely related to level of discomfort when administered prior to and one dose after a lumbar puncture (LP) +/- bone marrow biopsy (BM)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Children's Hospital of Eastern Ontario (CHEO) Research Ethics Board (ref: 09/10E). Approval pending as of 31/03/2009.

Primary study design
Interventional

Study design
Randomised controlled single-centre trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Haematological malignancy

Interventions
Cohort receives oral celecoxib 10 mg/kg 3 hours prior to first scheduled LP (LP 1) and then 5 mg /kg 12 hours after first dose and multiple blood samples to create blood PK profile.
Randomisation into one of two groups (Group 1: CSF dose timing; Group 2: dose variation) prior to undergoing the remaining scheduled LPs (LPs 2-5).

Group 1: Oral celecoxib 10 mg/kg either 60, 120, 300 or 900 mins prior to remaining 4 LPs followed by 5 mg/kg post first dose to create CSF PK profile.

Group 2: Either oral celecoxib 6 mg/kg or 14 mg/kg on 2 occasions each 3 hours before LP and then 12 hours later to create truncated CSF and blood PK profiles at higher and lower doses.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Celecoxib

Primary outcome(s)
1. All patients and CSF dose timing cohort (Group 1: Oral celecoxib 10 mg/kg pharmacokinetic profile)
1.1. Mean total and unbound plasma concentration ug/L at approximately the following time intervals (mins): 30, 60, 90, 120, 180, 300, 900
1.2. Mean CSF concentration ug/L at approximately the following time intervals (mins): 60, 120, 180, 300, 900
1.3. Ratio CSF/unbound plasma concentration at approximately the following time intervals (mins): 60, 120, 180, 300, 900
1.4. This information will be used to determine plasma and CSF mean +/- SD values for maximum concentration (Cmax [ug/L]); area under concentration curve from time 0 to infinity; apparent oral volume of distribution (Vd/F [L/kg]); apparent oral clearance (CL/F [L·h-1·kg-1] and terminal elimination half-life (t1/2 [h]). A median value will be determined for time to maximum concentration (tmax[h]).

2. Dose escalation cohort (Group 2: Oral celecoxib 6 mg/kg and 14 mg/kg pharmacokinetic profile)
2.1. Mean total and unbound plasma concentration ug/L at approximately the following time intervals (mins): 60, 180, 300
2.2. Mean CSF concentration ug/L at approximately 180 min
2.3. Ratio CSF/unbound plasma concentration at approximately 180 min
2.4. This information in conjunction with the pharmacokinetic profile established in the dose timing cohort (10 mg/kg) will be used to predict plasma and CSF values for tmax, Cmax, AUC, Vd /F, CL/F and t1/2 for 6 and 14 mg/kg oral doses respectively.

Key secondary outcome(s)
1. Polymorphisms of genotypes CYP2C9 and CYP3A4 liver enzymes and correlations to drug levels
2. Pediatric Quality of life Inventory (PedsQL) version 4.0 scores before and 7 days after LP
2.1. Parent report for children aged 2-7, 8-12 and 13-18
2.2. Child report ages 8-12 and 13-18
3. PedsQL Cancer module version 3.0 scores before and 7 days after LP
3.1. Parent report for children aged 2-7, 8-12 and 13-18
3.2. Child report ages 8-12 and 13-18
4. PedsQL Multidimension Fatigue Scale version 1.0 scores before and 7 days after LP
4.1. Parent report for children aged 2-7, 8-12 and 13-18
4.2. Child report ages 8-12 and 13-18
5. PedsQL Pediatric Pain Questionnaire baseline and daily scores for 7 days after LP
5.1. Parent report for children aged 2-7, 8-12 and 13-18
5.2. Child report ages 5-7, 8-12 and 13-18
6. Demographics including professional identity of the individual performing the LP+/-BM, description of the LP and BM needles used, number of attempts and degree of difficulty
7. Adverse events recorded daily for 7 days after each dose ingested

Completion date
01/10/2011

Eligibility

Key inclusion criteria
Both males and females, age 2-18 years with haematological malignancy expected to undergo five lumbar punctures.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 Years

Upper age limit
18 Years

Sex
All

Key exclusion criteria
1. Serum creatinine >2 X upper normal limit (UNL)
2. Abnormal liver function; namely alanine aminotransferase (ALT) >1.5 X UNL, alkaline phosphatase (ALP) > 5X UNL, total bilirubin >2 X UNL
3. History of peptic ulcer disease
4. Allergy to celecoxib, sulfonamide compounds or non steroidal anti-inflammatory drugs (NSAIDs)
5. Patients receiving CYP2C9 inhibitors fluconazole, amiodarone and oxandrolone
6. Patients receiving CYP2C9 inducers rifampin and phenobarbitol
7. Extremes of body mass index (BMI) (age related below 10th or above 90th percentile)
8. Parents of any participants, irrespective of age, who are unable to read and understand instructions relayed in English or French
9. Participant and/or parents of any participants, irrespective of age, who suffer from dementia, psychosis, significant developmental delay or other impairment that would prohibit the understanding and giving of informed consent or assent or the participation in self-care or toxicity reporting

Date of first enrolment
01/04/2009

Date of final enrolment
01/10/2011

Locations

Countries of recruitment

Canada

Study participating centre
Children's Hospital of Eastern Ontario
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Sponsor information

Organisation
Children's Hospital of Eastern Ontario Research Institute (Canada)

ROR
https://ror.org/05nsbhw27

Funder(s)

Funder type
University/education

Funder Name
University of Ottawa, Department of Anesthesiology, Chairman's Fund (Canada)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration