The effect of acetylcysteine on thiopurine use related liver injury.

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Thiopurine induced hepatotoxicity is related with an enhanced state of oxidative stress and may ameliorate after N-acetylcysteine supplementation.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21974

Bron
NTR

Verkorte titel
NACTOX

Aandoening

Inflammatory bowel disease; IBD; Crohn's disease; de ziekte van Crohn; ulcerative colitis; colitis ulcerosa; thiopurines; oxidative stress; hepatotoxicity; levertestafwijkingen

Ondersteuning

Primaire sponsor: VU University Medical Center
Overige ondersteuning: Fund=initiator=sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Change in liver tests.

Toelichting onderzoek

Achtergrond van het onderzoek

Thioprunes are pivotal in the treatment of inflammatory bowel disease such as Crohn's disease and ulcerative colitis. However, toxicity is a frequent cause of therapy cessation. Hepatotoxicity due to thiopurine therapy may be initiated by an increased state of oxidative stress due to the metabolization of thiopurines on one hand and due to low availability reduced glutathion and its amino acid precursors. By supplementation of N-acetylcysteine we try to reduce oxidative stress and thereby ameliorate hepatotoxicity.

Doel van het onderzoek

Thiopurine induced hepatotoxicity is related with an enhanced state of oxidative stress and may ameliorate after N-acetylcysteine supplementation.

Onderzoeksopzet

Elligible patients will be screened prior to defenite inclusion. After inclusion they will be randomly assigned to one of the two groups and will visit the outpatient clinics five times with an interval of four weeks. During the first eight weeks thiopurine therapy will be continued and depending on the group patients will concomitantly receive N-acetylcysteine 2400mg daily during weeks 1 to 4 or weeks 5 to 8. Weeks 9 to 12 both thiopurine therapy and N-acetylcysteine will be withdrawn. Rechallenge of solely thiopurine therapy takes place during weeks 13 to 16.

Onderzoeksproduct en/of interventie

Continuation of thiopurine treatment during eight weeks. During four weeks 600mg N-acetylcysteine effervescent tablets four times daily.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Crohn's disease and ulcerative colitis;

2. Patients between 18 and 70 years old;

3. Thiopurine use (azathioprine, 6-mercaptopurine or 6-thioguanine) for at least eight consecutive weeks;

4. Grade 1 or 2 toxicity on the CTCAEv3.0 of at least one of the folowing liver tests: ALAT, ASAT, gamma-GT, alkaline phosphatase and bilirubine.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Serological findings consistent with auto-immune or viral hepatitis (Hep A,B,C; EBV; CMV);

2. Currently known liver disease;

3. History of chemotherapy;

4. Ultrasonographic findings consistent with cholestasis;

5. Lactation or pregnancy;

6. 6-TGN concentrations above 1200 pmol/8x10*8;

7. Use of antioxidants during thiopurine therapy.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-06-2009
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	25-05-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1723
NTR-old	NTR1833
Ander register	MEC VUMC : 2009/56
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten
N/A