

# Determinants of thiazide induced hyponatraemia in pre-exposed elderly-a controlled experiment

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Thiazide-induced hyponatremia is caused by impaired free water excretion either due to alterations in the ADH-AVPR2-AQP2 pathway or impaired renal sodium handling.

|                             |                          |
|-----------------------------|--------------------------|
| <b>Ethische beoordeling</b> | Niet van toepassing      |
| <b>Status</b>               | Werving nog niet gestart |
| <b>Type aandoening</b>      | -                        |
| <b>Onderzoekstype</b>       | Interventie onderzoek    |

## Samenvatting

### ID

NL-OMON28630

### Bron

NTR

### Aandoening

hyponatraemia, elderly, sodium level, Thiazide

dutch: hyponatremie, ouderen, natrium, thiazide

## Ondersteuning

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**Overige ondersteuning:** Dutch Kidney Foundation

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Effect of a single oral dose hydrochloorthiazide 50 mg intake on the serum and urine sodium, serum ADH, prostaglandin E2 and urinary aquaporin-2 excretion in elderly patients (aged 60-80 years) with previous thiazide-induced hyponatraemia (sodium <125 mmol/l) without another cause for their hyponatraemia and matched controls receiving a thiazide diuretic without hyponatraemia.

Urinary hydrochlorothiazide concentrations are measured to analyse differences in thiazide metabolism. The response to ADH will be assessed by expression of AVPR2 in a cell-culture and determine its activity by measurement of cAMP

## Toelichting onderzoek

### Achtergrond van het onderzoek

Background: Thiazide diuretics are widely used for the treatment of hypertension, they are effective, cheap and generally well tolerated. In elderly patients, hyponatremia frequently complicates the use of thiazide diuretics and, when severe, can lead to loss of consciousness, coma and even death. It cannot be predicted in who, or when, this serious complication will develop as the mechanisms resulting in thiazide-induced hyponatremia are unclear. Impaired free water excretion is thought to be primarily responsible for thiazide-induced hyponatremia. Decreased sensitivity of osmoreceptors, activating mutations in the ADH-receptor (AVPR2) or aquaporine-2 (AQP2) gene, decreased renal prostaglandin availability or impaired renal sodium handling as a result of mutations in thiazide- and amiloride-sensitive sodium channels may all be responsible for thiazide-induced hyponatremia. In the proposed trial we aim to elucidate the mechanisms underlying thiazide-induced hyponatremia and try to identify patients who are at risk of this potentially fatal complication by means of a controlled experimental study Hypothesis: Thiazide-induced hyponatremia is caused by impaired free water excretion either due to alterations in the ADH-AVPR2-AQP2 pathway or impaired renal sodium handling.

Patients and methods: a controlled experimental study comparing 18 elderly patients (aged 60-80 years) with previous thiazide-induced hyponatremia (sodium <125 mmol/l) and matched controls receiving a thiazide diuretic without hyponatremia. Before the experiment thiazides are stopped. During the experiment patients and controls receive a single dose of hydrochlorothiazide. Serum and urine sodium, serum ADH, urine AQP2 and prostaglandin E2 are determined to evaluate the response to hydrochlorothiazide. Urinary hydrochlorothiazide concentrations are measured to analyse differences in thiazide metabolism. Fluid balance will be monitored under ad libitum water drinking conditions. The response to ADH will be assessed by expression of AVPR2 in a cell-culture and determine its activity by measurement of cAMP.

## Doel van het onderzoek

Thiazide-induced hyponatremia is caused by impaired free water excretion either due to alterations in the ADH-AVPR2-AQP2 pathway or impaired renal sodium handling.

## Onderzoeksproduct en/of interventie

All subjects included in this controlled experiment will receive a single dose of Hydrochloorthiazide 50 mg. After that they will be monitored for 24hours

## Contactpersonen

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### Wetenschappelijk

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## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age 60-80 years;
2. Previously admitted with thiazide-induced hyponatraemia;
3. Patients must be willing and medically able to discontinue anti-hypertensive therapy six weeks before the study and for the duration of the study;
4. Patients must be willing to be admitted for 24 hours and must be medically able to take

the study medication;

5. Patients must be willing to give informed consent.

## **Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)**

1. Other causes for hyponatraemia (e.g. heart failure, pulmonary disease, medication associated with hyponatraemia);
2. Renal dysfunction (estimated clearance <50 ml/min according to Cockcroft-Gault);
3. Liver cirrhosis;
4. Heartfailure;
5. Medication: antidepressiva (SSRI's), antiepileptica, prednisone, NSAID's, opioids, other diuretics (e.g. lasix, burinex, chloorthalidon, dytac);
6. Allergy for sulfonamidederivaten;
7. Therapy resistant hypertension (BP>140/90 mmHg while using 3 or more anti-hypertensive drugs)

## **Onderzoeksopzet**

### **Opzet**

|                  |                         |
|------------------|-------------------------|
| Type:            | Interventie onderzoek   |
| Onderzoeksmodel: | Parallel                |
| Blinding:        | Open / niet geblindeerd |
| Controle:        | Geneesmiddel            |

### **Deelname**

|                         |                          |
|-------------------------|--------------------------|
| Nederland               |                          |
| Status:                 | Werving nog niet gestart |
| (Verwachte) startdatum: | 01-08-2007               |
| Aantal proefpersonen:   | 36                       |
| Type:                   | Verwachte startdatum     |

## **Ethische beoordeling**

Niet van toepassing

Soort:

Niet van toepassing

## 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        | NL968          |
| NTR-old        | NTR995         |
| Ander register | :              |
| ISRCTN         | ISRCTN38727701 |

## Resultaten