



# ENCEPHALOPATHY DUE TO PROLONGED MISUSE OF IVERMECTIN (STROMEKTOL®) AFTER SCABIES INFECTION.

DERAEMAER CATHERINE (1), FERRAO SUSANA (2), GOOSSENS ELISABETH (1), MOSTIN MARTINE (1), SINDIC CHRISTIAN (2). 1. BELGIAN POISON CENTRE, BRUSSELS, BELGIUM; 2.SERVICE DE NEUROLOGIE, CLINIQUES UNIVERSITAIRES SAINT-LUC, BRUSSELS, BELGIUM.

## DESCRIPTION OF A CASE OF CHRONIC IVERMECTIN OVERDOSE RESULTING IN ENCEPHALOPATHY.

### IVERMECTIN: DESCRIPTION AND PLACE IN THERAPY

Ivermectin is a semisynthetic antiparasitic drug of the avermectin class. It is the mixture of 22,23-dihydro-avermectin B1a (at least 90%) and 22,23-dihydro-avermectin B1b (less than 10%). The avermectins are produced by fermentation of *Streptomyces avermitilis*. (Ref 1). Ivermectin is used in the treatment of parasite infestations by invertebrate (nematodes and insects) in veterinary and human medicine.

In invertebrate, Ivermectin binds selectively to glutamate-gated chloride ion channels in muscle and nerve cells and causes an increase in the permeability of the cell membrane to chloride ions. This leads to paralysis and death of the parasite (Ref 1).

In vertebrates, Ivermectin can affect the central nervous system through reactions at the receptor for the gamma-aminobutyric acid (GABA) neurotransmitter. Ivermectin acts as a GABA receptor agonist (Ref 2).

In humans, Ivermectin is used in the treatment of parasitic infection like onchocerciasis or strongiloidosis. In some countries, it is also approved by oral route for the treatment of scabies and for the topical treatment of head lice infestations.

### CASE REPORT

For the treatment of scabies, a 41-year-old woman was prescribed one single dose of four 3mg Ivermectin tablets in January.

Because of persistent pruritus on hands and feet, she consulted several dermatologists and one neurologist between April and October, in the same outpatient clinic. She also consulted the Institute of tropical medicine and most probably other practitioners.

She obtained multiple prescriptions of Ivermectin tablets and repeated the intake of 4 tablets every week during 6 months. She was also prescribed local treatment with Crothamiton and Permethrin based lotion and cream.

Parasitophobia was suspected after 2 months of repeated consultations as the patient felt moving cysts in her belly and described little beasts crawling on her skin. She declined psychiatric help.

Two weeks before admission, she increased the Ivermectin dosage to 4 tablets a day. She was brought to the Emergency Department by her husband because of vertigo, somnolence, speech problems and abnormal movements of 4 days duration. Her husband said that she was confused and disoriented in time. On examination, she was effectively confused and apathic, with a slow and dysarthric speech. She presented myoclonia of the hands. The EEG showed generalized slowing and depressed reactivity. The CT scan and the MRI were within normal limits. The dermatologist confirmed the absence of scabies and the presence of scratch lesions on hands and feet.

The patient didn't take Ivermectin on the day of admission. She was advised to immediately stop Ivermectin and she was treated with Cetirizine against pruritus. Two days after stopping Ivermectin, the neurological symptoms improved. The victim could leave the hospital 3 days after the last Ivermectin intake.

### PHARMACOKINETICS

By oral route, Ivermectin is moderately well absorbed and the absorption increases proportionally when the dose raises. A high fat meal improves the absorption. The volume of distribution is 3 to 3.5 L/kg. Ivermectin does not cross the blood-brain barrier at therapeutic dose. Protein binding is 93%. The metabolism is primarily hepatic. Ivermectin and its metabolites are excreted almost exclusively in the feces. Less than 1 % of the administered dose is excreted in the urine. The half-life of the parent compound is about 12 hours (Ref 3).

### DISCUSSION

In mammals, Ivermectin can bind to the GABA type A gated chloride channels (GABA A receptors) that are only present in the CNS. P-glycoprotein, a component of the Blood Brain Barrier (BBB), transports some substances, including Ivermectin, back across the cell membranes. Some breed of dogs (collie, sheltie, Australian shepherd) have a defect in the ABCB1 gene that results in a lack of functional P-glycoprotein. Cases of Ivermectin poisoning with severe CNS symptoms have been described in these dogs at therapeutic dose.

In human, Ivermectin doesn't cross the BBB and no central nervous system toxicity has been described at therapeutic dose. However CNS toxicity can occur in acute or chronic overdose.

Kong Chung and all (Ref 4) described a case of a 61 year old woman who developed a deep coma with decreased tendon reflexes after accidental ingestion of 100 mL 1% Ivermectin solution.

Our patient was exposed to supratherapeutic doses of Ivermectin during several months: 12mg/week during at least six months followed by 12 mg daily during 2 weeks. She developed an encephalopathy after approximately 10 days of this extensive daily regimen.

We found a similar case report in the literature: Debonis and all (Ref 5) described a case of ataxia, slow speech and tremor after repeated daily intake of Ivermectin in a psychotic 46 y old patient. Like in our patient, Ivermectin was taken on self-initiative to cure symptoms of cutaneous itching attributed to unsubstantiated parasitic infestation. Symptoms resolved after 2 days of supportive care.

It is well known that pruritus is a long lasting symptom after scabies infestation and is not a sign of persisting infection.

In our patient, the additional topical use of a permethrin solution on the hands may have exacerbated the paresthesia and led to Ivermectin abuse.

Reassurance of the patient and good information about possible persisting pruritus after scabies treatment is important to avoid Ivermectin misuse.

### REFERENCES

1. Martindale, The Complete Drug Reference, in Truven Health Analytics Inc. MICROMEDEX(R) Healthcare Series Vol. 160 expires 6/2014
2. Robert I Krieger, Handbook of Pesticide Toxicology, Academic Press, 2001.
3. Stromectol® Product Information, Merck Sharp & Dohme-Chibret, Paris, France.
4. Kong Chung and all, Agricultural Avermectins: an uncommon but potentially fatal cause of pesticide poisoning, Annals of Emergency Medicine, 1999, 34:1, 51-57.
5. Debonis K and all, Psychosis, Ivermectin toxicity and "Morgellons Disease", Psychosomatics, 2011, 52:3, 295-296.



070 245 245