

The risks of self-medication: case report of familial misuse of AM3 (Immunoferon®)

Marta Oliveira, Rute Neves, Margarida Abranches

Paediatric Nephrology Unit, Department of Paediatrics, Hospital Dona Estefânia. Lisboa, Portugal.

Received for publication: 13/05/2010

Accepted in revised form: 20/08/2010

■ ABSTRACT

Over the last decades extended medical knowledge has been an important health care benefit in terms of disease prevention and management. However, probably with no exception, most pharmaceutical products are not devoid of adverse consequences.

Immunomodulators are commonly considered a “benign” drug whose advantages bypass consequences. The immunomodulator AM₃ (Immunoferon®) is a clinically used, orally administered compound whose active principle is stabilised in an inorganic matrix of calcium.

We report the misuse of AM₃ in three members of a family; father and two children. The drug was prescribed to the father who subsequently administered it to the children without seeking medical advice. Two months later, all subjects developed abdominal and/or flank colicky pain. Hypercalciuria was diagnosed in the children with different degrees of severity. It is likely that the calcium content of the inorganic matrix played an important role in the onset of symptoms.

No adverse side effects related to the inorganic matrix of calcium of immunoferon® have been documented so far. This family case report calls attention to the risks of self-medication in a susceptible family.

Paediatric patients are vulnerable as they rely on adults for the supply of medications. Concerning the

use of drugs in family, especially nonprescription drugs, the quality of health care provided to the children depends on the health literacy of their parents.

Key-Words:

Hypercalciuria; Immunoferon; self-medication.

■ INTRODUCTION

Self-medication (SM) can be seen as a modern style of self-care which is increasing in developed countries. Some social factors may be considered important causes behind this rise of SM, such as the decrease in prescription coverage by National Health/social security services, the availability of over-the-counter health products and the increasing presence of pharmaceutical products in the media^{1,2}.

Immunoferon (AM₃) is an orally effective immunomodulator which influences regulatory and effectors functions of the immune system and whose molecular mechanism of action is mostly unknown. The active principle is a glycoconjugate of natural origin composed of glucomannan polysaccharide from *Candida utilis* and a storage protein from non-germinated seeds of *Ricinus communis*³. Its use in adults and children with chronic lung disease and asthma is documented^{4,5}.

Immunoferon® is available in 500mg capsules containing glycopeptides/protein stabilised in an

inorganic matrix of calcium phosphosulfate (10 mg AM₃ and 490 mg calcium phosphosulfate).

■ CASE REPORT

Female, 11 years old, complained of fever, abdominal pain and diarrhoea. Two days later she was admitted to the emergency services with an abdominal colicky pain irradiating to the right flank. Urine sediment and urine culture were normal. An abdominal ultrasonography showed an enlarged right kidney with diffuse hyperechogenicity of the cortex and dilatation of the renal pelvis (28mm) and of the homolateral ureter (8mm). Contrast-enhanced computed tomography scanning revealed right ureterohydronephrosis with diminished uptake, concentration and excretion of the ionising contrast and a normal left kidney. Cystoscopy was performed and revealed obstruction at the third distal portion of the right ureter. Reimplantation of the right ureter and insertion of a stent was successfully performed. A sandy-like material causing the obstruction was removed and not sent for analysis. During recovery, serum creatinine and urea were normal (Screatinine 0.9 mg/dl, Surea 40 mg/dl), urine biochemistry only revealed hypercalciuria (CaU/CrU=0.3); other serum biochemistry parameters including serum calcium were normal (SCa 9.3 mg/dl). Hypercalciuria normalised spontaneously. She was followed up for four consecutive years: blood and urine biochemistry were always normal, serial renal ultrasonograms showed no lithiasis and dynamic renal scintigraphy showed normal renal function with no significant asymmetries and without dilatation of the right urinary tract.

One week after her hospital admission, while recovering from the urological surgery, her brother, aged three, was also admitted to the emergency services with an abdominal colicky pain. Analgesic and intravenous fluid therapy kept the pain under control. Abdominal and renal ultrasonography were normal. Urine sediment, urine culture and blood biochemistry, including serum calcium, showed no alterations. Chemical analysis of the urine consistently revealed hypercalciuria (UCa 6-10mg/kg/day), and other urine chemical parameters were normal. A low sodium diet and high fluid intake were not enough to manage the hypercalciuria and hydrochlorothiazide was successfully introduced. Serial renal

ultrasonograms never revealed lithiasis. Currently aged 11, he is still under surveillance.

The family was questioned as to dietary habits and medications. A three-day diet report was requested, and its calcium intake was evaluated and considered normal. No vitamins or calcium supplements were being given to the children. However, their father mentioned taking Immunoferon[®] and self-administering it to his children. He admitted that Immunoferon[®] had been prescribed for prevention of his recurrent upper respiratory infections nine months before his children's hospital admissions. He took the medication as prescribed, 500mg three times a day, for three consecutive months, and used the same drug as self-medication, a second time, two months prior to the hospitalisations. This last time, he decided to administer it to both his children without seeking medical advice. Moreover, he had two episodes of colicky flank pain which had resolved spontaneously. His last episode occurred two weeks prior to his children's hospital admissions. When questioned, he refused to test his urine and blood for calcium content.

■ DISCUSSION

Over the past three decades, there has been a tremendous rise in available treatments as a result of extended medical knowledge. The prevalence of non-prescription drug use is rising in the world, as is the potential for therapeutic misuse. All prescription and nonprescription drugs are powerful chemical entities with well-defined pharmacology and toxicology^{6,7}.

Various definitions of SM are available in the literature as well as various prevalence studies of SM with different results from different countries. In Portugal, two prevalence studies were carried out in urban and rural populations with results of 26.2% and 21.5% respectively^{8,9}. In Spain, prevalence of SM in a sample representative of the Spanish population² was 12.7%. One must take into account that prevalence of SM in different countries is difficult to compare because there is no standard measurement of SM.

In this familial case report, there seemed to be a cause-effect relationship between the administration of a self-medicated drug, Immunoferon[®], and the

occurrence of colicky pain in three family members. In this case, calcium content of the inorganic matrix of Immunoferon® probably played an important role. Although the package leaflet of Immunoferon® calls attention to the risks of administration in cases of hypercalcaemia, there is no reference to hypercalciuria. Furthermore, a previous undiagnosed urinary tract anomaly in the daughter could possibly justify the severity of the unilateral urologic obstruction in need of surgical repair. Regarding her brother, a colicky pain episode probably disclosed a previous undiagnosed hypercalciuric state. Their father's report of two colicky pain episodes, both concomitant with administration of Immunoferon®, were not fully explained since laboratory tests were not performed.

Calcium metabolism depends on the calcium content of the diet, the absorption from the gut and the tubular reabsorption of the kidney. A diminished renal tubular reabsorption increases the excretion of calcium and induces a hypercalciuric state. In cases of hypercalciuria induced by diminished tubular reabsorption of calcium, any overload of calcium, dietary or iatrogenic, will increase the excretion of calcium and enhance a hypercalciuric state. Thiazide diuretics reduce renal excretion of calcium by increasing calcium tubular reabsorption as in our case. The most common cause of hypercalciuria is idiopathic but it can be familial, hence the importance of knowing the calcium metabolism of all the family members with colicky symptoms.

As shown by this family case report, the use of nonprescription drugs calls for the health literacy of patients and caregivers¹⁰. There are population groups with special needs, with paediatric patients among the most vulnerable due to age considerations and dependency on adults to supply the medication.

Conflict of interest statement. None declared.

References

1. Blenkinsopp A, Bradley C. Patients, society and the increase in self-medication. *Br Med J* 1996;312:629-632
2. Figueiras A, Caamaño F, Gestal-Otero JJ. Sociodemographic factors related to self-medication. *Eur J Epidemiol* 2000;16:19-26
3. Varela J, Navarro Pico ML, Guerrero A, *et al.* Identification and characterization of the peptidic component of the immunomodulatory glycoconjugate Immunoferon. *Methods Find Exp Clin Pharmacol* 2002;24:471-480
4. Martín ER, Almendros CF, Álvarez-Sala JL, Álvarez-Mon M. Efecto del inmunomodulador AM3 sobre las agudizaciones en enfermos con bronquitis crónica: una revisión sistemática de estudios controlados. *Rev Clin Esp* 2004;204:466-467
5. Sanchez Palacios A, García Marrero JA, Schamann F. Immunological clinical evaluation of a biological response modifier, AM3, in the treatment of childhood infectious respiratory pathology. *Allergol Immunopathol* 1992;20:35-39
6. De Bolle L, Mehuys E, Adriaens E, *et al.* Home medication cabinets and self-medication: a source for potential health threats? *Ann Pharmacother* 2008;42: 572-579
7. Covington TR. Nonprescription medications and self-care: Issues and opportunities. *Am J Pharm Educ* 2006;70:137
8. Martins AP, Miranda AC, Mendes Z, *et al.* Self-medication in a Portuguese urban population: a prevalence study. *Pharmacoepidemiol and drug safety* 2002;11:409-414
9. Nunes de Melo M, Madureira B, Ferreira APN, *et al.* Prevalence of self-medication in rural areas of Portugal. *Pharm World Sci* 2006;28:19-35
10. Rothman RL, Yin S, Mulvaney S, *et al.* Health literacy and quality: focus on chronic illness care and patient safety. *Pediatrics* 2009;124:S315-S326

Correspondence to:

Dr Margarida Abranches
Paediatric Nephrology Unit
Hospital Dona Estefânia
R. Jacinta Marto,
1169-045 Lisboa, Portugal
E-mail: margarida.abranches@gmail.com