CASE REPORT: RARE ADVERSE REACTION OF A NONSTEROIDAL ANTI-INFLAMMATORY DRUG IN A PRIVATE PILOT RISK OF SELF MEDICATION

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I have no financial relationships to disclose.

I will discuss the particular medication relating to this case presentation.

The medicine that is mentioned in this document under its generic name is used by million of patients.

The purpose of this presentation is not to doubt its efficiency or beneficial effects.
INTRODUCTION

CLINICAL REPORT

Inform about a rare side effect of a currently used medicine

Remember that the use of an ordinary drug is not always without danger

Example of a treatment with ibuprofen

Problem of self-medication with pilots

A problem for flight safety?
CASE REPORT - 1

Woman, 40 years old, doctor and private pilot.

PMH:
- ex-smoker, quit 4 years previously
- tonsils removed as a child

Way of life: travels often

9 days after a vacation in Corsica:
Viral rhinopharyngitis → paracetamol 500 mg x 3 / day
3 days later: fever of 38.5°C then 39.8°C, sinusitis with clear secretions:
  → paracetamol: 1 gram x 3 / day
  → ibuprofen 200 mg + pseudoephedrine 30 mg bd 2 days
6 days later: headache + nausea
Symptoms on the 7th day: $T^\circ = 38.7^\circ$

Headache:
- intolerable
- all over the head, but primarily in the front
- jarring pain when walking; had to shuffle her feet to avoid intensifying the headache

Nausea intensifies, not vomiting

Photophobia: no

Neck stiffness: no...

... But stiffness of the back!

Self diagnosis of meningitis(?)

Urgent hospitalization
At the hospital:
**Echocardiography:** Normal
**CT Brain scan:** Normal

**Biological tests:** no evidence of infection or inflammation

**White blood cells:** low and CRP not significant

**Spinal tap:** protein 0.50 g/l; glucose 2.9 mmol/l
258 cells/mm³ (75% neutrophils, 15% lymphocytes, 10% other cells). 3 red blood cells/mm³.

Doubt on the existence of 2 bacteriae. **Negative cultures.** Meningitis confirmed.
Rest of the tests: all negative

Tests for infections: negative

Serology: negative

Detection of auto immune diseases: negative
TREATMENT: cefotaxime, vancomycin, gentamicin, dexamethasone, ivermectin, paracetamol.

Progression on the 8th day
1) Toxiderma
2) Thrombocytopenia at 8000/mm³ with hemorrhage and purpura, with bullae in mouth and throat.

FURTHER TREATMENT:
Cessation of antibiotics and paracetamol → Nefopam
Transfusion of platelets
Perfusion of immunoglobulin 1g/kg (IgPVIV)
Aseptic meningitis due to ibuprofen

→ indication against NSAIDs, especially to « propioniques », which are definitely forbidden

Toxiderma and thrombocytopenia
« due to vancomycin »

→ indication against glycopeptides :
Glycopeptides are definitely forbidden
→ Beware ! Cefotaxime and paracetamol can eventually be responsible for these complications.
FOLLOW UP

Asthenia during a few weeks

Recuperation without sequelae

Then...

... After medical examination
And obtaining a new certificate of aptitude Class 2
Back to flying without restriction

*****

Three months later...
Skin tests (patch) : negative
Other tests : refused
Immuno-allergic mechanism is sometimes at the origin of a meningitis, appearing a few days after taking a drug and decreasing rapidly after stopping the drug.

- Diagnosis by process of elimination
- Atypical symptoms are possible
- Predominance of neutrophils: 50% of cases, sometimes lymphocytosis or eosinophilia
- CONNECTIVE TISSUE DISEASES/ SYSTEMIC LUPUS ERYTHEMATOSIS
- NSAIDs the most often involved; IBUPROFEN the most often found (31 cases reported in 2002)
  Also: antibiotics, anticlonal mononuclear antibodies anti-CD3, or Immunoglobulins...
QUESTIONS ? - 1

Use of ibuprofen: true case of self medication?
1°) doctor
2°) no excessive use of drug (no antibiotics)

Complications due to the second treatment in hospital?
1°) were as unexpected as the previous ones
2°) consequences of the justified prescription by a reputable medical team

► A properly prescribed drug can also lead to severe adverse effects.
3°) is it linked to immunological disturbance due to the previous intake of ibuprofen?? No one knows.
Any treatment is likely to generate side effects.

WHEN?

- The moment is unpredictable...
  - after the intake of the first tablet?
  - 2 days after a 48 hour treatment?
  - after 20 years of use?

WHERE?

- In the vicinity of a hospital? In hospital?
- On a plane? Flight safety?

BUT:
- heavy advertising of drugs (TV);
- failure to disclose drug use by the pilot for fear of losing licence
RISKS: THE EXAMPLE OF IBUPROFEN

DIGESTIVE
Nausea, epigastric pain, vomiting, dyspepsia, diarrhea, *gastric bleeding*, gastric ulcer, perforation and frank hemorrhage of digestive system

ALLERGY
Pruritis, cutaneous eruptions, Quinck’s edema, asthmatic risis, anaphylactic shock, bullous dermatoses

NEUROLOGICAL
Vertigo, headache, eyesight problems, somnolence, tinnitus, fatigue, insomnia, *aseptic meningitis*

DIVERSE
Oedema, hypertension, hepatitis, *renal insufficiency*, oliguria, nephrotic syndrome, iatrogenic cystitis, anemia, leucopenia
IBUPROFEN IS USEFUL!

France: The « SMR, Service Médical Rendu », defined by the Health Authority according to the ratio benefits/risk of a drug, to the severity of the affliction to treat and to its place in the therapeutic strategy, to the nature of the treatment and the impact expected on public health, determines the reimbursement of the medicine.

<table>
<thead>
<tr>
<th>Relevance of the drug</th>
<th>Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important or major</td>
<td>65%</td>
</tr>
<tr>
<td>Moderate</td>
<td>30%</td>
</tr>
<tr>
<td>Weak</td>
<td>15%</td>
</tr>
<tr>
<td>Insufficient</td>
<td>No</td>
</tr>
</tbody>
</table>

Ibuprofen = 65%!
SELF PRESCRIBED MEDICINES

FAA

Aspirin
Ibuprofen
Antihistamines
Vasoconstrictors (pseudoephedrine)
Anti-tussive
Laxatives
Anti-diarrhea
Caffeine...

Effects on haemostasis, blood pressure, caution...
IATROGENIC :
SOME FIGURES - 1

In France

→ EMIR Study
(Undesirable effects of medicines = Incidence and Risk)
Lead by the network of the regional centers of Monitoring in 2007
- 143 915 hospitalizations
- 1 480 885 days of hospitalization

→ Report of the Commission of the Social Affairs of the Parliament in conclusion of the study of iatrogenic adverse effects:
- 150 000 hospitalizations / yr
- 13 000 to 18 000 deaths
Undesirable effects due to medicines:
- Twice more numerous in average after the age of 65
- 10 to 20 % of them lead to hospitalization
- Often the consequences:
  - Of therapeutic error
  - Of bad compliance with the treatment
  - Of inappropriate self medication

Medical consultation without prescription

Netherlands: 50 to 60 % of the patients / France: 10 to 25 %...
ROLE OF THE AME

Ask the appropriate questions to the pilot

*Anonymous investigation: JP Taillemitte, B Sicard and J. Deroche*

- 81% of the crew members use medicines
- 53% use self medication
- 19% don’t fear any danger

Inform about risks; can justify a decision to be unfit or a decision with a restriction to be fit

Advise: a new treatment may require a temporary interruption of flying
MED.A.020. Decrease in medical fitness

a) Licence holders shall not exercise the privileges of their licence and related ratings or certificate at any time when they:
   1) are aware of any decrease of their medical fitness...
   2) take or use prescribed or non prescribed medication which is likely to interfere with the safe exercise of the privileges of the applicable licence;
   3) receive any medical, surgical or other treatment that is likely to interfere with flight safety.

b) In addition, licence holders shall, without undue delay, seek aeromedical advice when they:
   2) have commenced the regular use of any medication....
The rarest side effects of a drug may happen.

Advise to avoid any intake of unnecessary medicine.

So…
DOCTOR: HIS ROLE IS TO INFORM +++
When someone asks for an unnecessary prescription, the doctor should say
THE PILOT: should be aware of the rules and also follow the advice of the doctor! Advising him is helping him to say.
THANK YOU FOR YOUR ATTENTION
Méningite aseptique récidivante due aux anti-inflammatoires non stéroïdiens chez une patiente lupique
Recurent aseptic meningitis secondary to nonsteroidal anti-inflammatory drugs in a patient with lupus
P. Faurie, L. Pérard, A. Hot, H. Desmurs-Clavel, T. Fassier, A. Boibieux, J. Ninet

Méningites chroniques
[ Article 17-160-C-30] - Groupe hospitalier Pitié-Salpétrière

Characteristics of meningitis caused by Ibuprofen : report of 2 cases with recurrent episodes and review of the literature
Rodriguez SC, Olguin AM, Miralles CP, Viadrich PF
Infectious Diseases Service, Hospital Universitari de Bellvitge, L’Hospitalet del Llobregat, Barcelona, Spain

Drugs and Alcohol Found in Civil Aviation Accident – Pilot Fatalities from 2004-2008
Dennis V. Canfield, Kurt M. Dubowski, Arvind K. Chaturvedi, and James E. Whinnery

Prise médicamenteuse dans le personnel navigant. Enquête anonyme chez 1000 pilotes. Premiers résultats.
Burlaton J.P, Gourbat J.P
Communication aux VIIème journées de médecine aéronautique. HIA Percy. Med. Aer. Spat. XXXVIII ; 150, 91-95
Effets secondaires des médicaments. Automédication. Hypnotiques, mélatonine et activité aéronautique
Communication aux journées de médecine aéronautique de Marseille. 8 octobre 1999
Med. Aer.Spat. 1999 XXXVIII n°152, 225-230

Emploi des médicaments qui perturbent la vigilance par les équipages de l’aéronautique
J.-P. Taillemite, B. Sicard, J. Deroche - Médecine aéronautique et spatiale – SOFRAMAS – Tome 43 – n°162/03