How to prevent iatrogenic risk? benzodiazepine dependence

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CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report
Plan

✓ Short reminders about benzodiazepine / dependence

✓ Prevention
  ✓ Doctor
  ✓ Patient
  ✓ Health Policy

✓ Treatment
Benzodiazepine

- First one in 1960
- Anxiolytic + hypnotic + muscle relaxant + anticonvulsivant + amnesic effects
- Drowsiness, attention problems, ataxia, falls, traffic accident
- Activation of GABA\(_\alpha\) receptor + indirect activation of dopaminergic neurons implicated in the reward circuitry

Opening of the chloride channel is potentiated by GABA agonists such as benzodiazepines
Dependence

✓ Dependence (physical) / Addiction (psychological)

✓ DSM 5 : substance use disorder (≥2/11)
  ✓ Tolerance
  ✓ Craving
  ✓ Withdrawal symptoms
  ✓ Continuing to use, despite negative consequences...
  ✓ ...

✓ « pseudo-therapeutic long term use »
Prevalence of long term use

✓ General population +/- 3%
  ✓ Strong association with age and female gender
  ✓ Possible association with Alzheimer diagnosis, Nursing home
  ✓ Family practitioner (especially oldest patient and long term use)

✓ Elderly patient
  ✓ USA (65-80) 2.7% (2008)
  ✓ Brazil: 14% (1997)
  ✓ Australia: 16% (2000)
  ✓ Europe: Germany 1% (2008-11)
    France +/- 25% (38% W>80ans; 2015)

✓ Evolution
  ✓ Increase in the US
  ✓ Decrease in Europe
État des lieux de la consommation des benzodiazépines en France. ANSM 2017
Médicaments psychotropes, consommations et pharmacodépendances, INSERM 2012

12/10/2017

Emetteur
✓ Short reminders about benzodiazepine / dependence

✓ Prevention
   ✓ Medical Education
   ✓ Patient attitude
   ✓ Health Policy

✓ Treatment
Medical education: What’s the problem with doctors?

- « Deserving » patients
  - Multimorbid old lady > alcoholic
  - Empathy
  - Palliative treatment

- Lack of alternative
  - Psychotherapeutic program
  - Psychiatric support
  - Powerlessness / complex psychosocial situation

- Anticipation of patient resistance
  - Question doctor competence

If we give people something and make them feel better, then everybody seems to be happier!

A quick fix: you don’t have time, that’s what they want!

Sirdifield et al, BMC Family Practice 2013
Patient’s attitude

✓ Negative impact of insomnia on health and quality of life + Failure of self care strategy
  Seek medical help

✓ Lack of support from the GP (short consultation time)
  ✓ Not enough dialogue
  ✓ Not enough information on drugs and alternative

✓ Trust the GP

✓ Necessity to maintain a normal life

“ I’m having marriage problem because of this thing of not sleeping ”

“ I’d eat a bucket of nails if you told me it would help me to sleep ”

Sirdifield et al, Patient 2017
Dialogue

✓ Discuss strategy of coping the patient has already try, to propose adequate alternatives to bzd

✓ Explore directly patient expectation

✓ Raise awareness about bzd side effects

✓ Ask the patient how he use his bzd, discuss circumstance of the initial prescription
Health Policy
What they could do...

- Improve access to cognitive behavioral therapy
- Create educational resources
  - Realistic expectation on sleep
  - Online cognitive behavioral therapy
- Organize personalized support delivered by healthcare professionals (nurses, pharmacist...)

European Academy for Medicine of Ageing
Health Policy
What they do (in France)...

✓ Make bzd prescription more time consuming for the GP
  - Limitation of the duration of prescription
    ✓ 4 weeks for hypnotics
    ✓ 12 weeks for anxiolytics
  - Zolpidem on a secured medication order

✓ Write new guidelines (3/10 years)
• Don’t use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation or delirium (USA, Canada, Australia, Switzerland)

• Non usare le benzodiazepine negli anziani come prima scelta per insonnia, agitazione, delirium (Italy)

• Benzodiazepine oder andere Sedativa beziehungsweise Hypnotika bei älteren Patienten sollen nicht als Mittel der ersten Wahl im Falle von Schlafstörungen, Agitation oder Delir eingesetzt werden(Germany)

• Il n’y a pas d’indication à un traitement prolongé par benzodiazépine. En cas d’usage ancien, l’intérêt d’un sevrage et les moyens d’y parvenir doivent être expliqués au patient (France)
✓ Short reminders about benzodiazepine / dependence
✓ Prevention
  ✓ Doctor
  ✓ Patient
  ✓ Health Policy

✓ Treatment
## Table 5. Management of Benzodiazepine (BZD) Withdrawal.

<table>
<thead>
<tr>
<th>Situation</th>
<th>Treatment Approach</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approach to BZD dependence in general</td>
<td>Gradual withdrawal over a period of several weeks or months</td>
<td>High</td>
</tr>
<tr>
<td>Use of several BZDs or sedatives</td>
<td>Switch to use of only one BZD for detoxification (diazepam)</td>
<td>Good</td>
</tr>
<tr>
<td>Choice of BZD for detoxification</td>
<td>Switch to a long-acting BZD (diazepam)</td>
<td>Low</td>
</tr>
<tr>
<td>BZD withdrawal in a patient receiving opioid maintenance therapy</td>
<td>Adjustment of opioid dose to prevent opioid withdrawal; switch to a partial agonist (buprenorphine)</td>
<td>Good for adjustment of opioid dose; moderate for switch to partial agonist</td>
</tr>
<tr>
<td>Concomitant pharmacotherapy for BZD withdrawal</td>
<td>Carbamazepine, 200 mg twice a day</td>
<td>Moderate</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>Antidepressants, antihistaminergic drugs, melatonin; improved sleep hygiene, sleep restriction, relaxation techniques</td>
<td>Moderate</td>
</tr>
<tr>
<td>Other drugs for treatment of withdrawal symptoms</td>
<td>Pregabalin, gabapentin, beta-blockers; flumazenil</td>
<td>Low for pregabalin, gabapentin, and beta-blockers; experimental for flumazenil</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>Cognitive behavioral therapy and other approaches</td>
<td>Good</td>
</tr>
</tbody>
</table>
Intervention

✓ Written information as efficient as follow up visit
  ✓ 532 patients / 75 GP in Spain
  ✓ Educational interview (20 min) + follow up (12 min) or written instruction and information
  ✓ 45% achieved complete withdrawal
  ✓ Transitory withdrawal symptoms: tremor (+10%), irritability (+15%), insomnia (+30%), anxiety (+17%)

  

Vicens et al, BJGP 2016

✓ EMPOWER brochure
  ✓ 261 participants (65-95) / 30 pharmacies in Canada
  ✓ A 8-page booklet (mailed)

Tannenbaum et al, JAMA Intern Med. 2014
You May Be at Risk.

TEST YOUR KNOWLEDGE

1. Ativan® is a mild tranquilizer that is safe when taken for long periods of time.
   True □ False □

2. The dose of Ativan® that I am taking causes no side effects.
   True □ False □

3. Without Ativan® I will be unable to sleep or will experience unwanted anxiety.
   True □ False □

4. Ativan® is the best available option to treat my symptoms.
   True □ False □

(Answers are found on the next page.)

Mrs. Robinson’s story

“I am 65 years old and took Ativan® for 10 years. A few months ago, I fell in the middle of the night on my way to the bathroom and had to go to the hospital. I was lucky and, except for some bruises, I did not hurt myself. I read that Ativan® puts me at risk for falls. I did not know if I could live without Ativan® as I always have trouble falling asleep and sometimes wake up in the middle of the night.”
Intervention

✓ EMPOWER brochure
  ✓ 261 participants (65-95) / 30 pharmacies in Canada
  ✓ A 8-page booklet (mailed)
  ✓ 27% achieved complete withdrawal
  ✓ lack of support from a healthcare provider!
  ✓ Same rate in adults with MCI

Tannenbaum et al, JAMA Intern Med. 2014
Conclusion

✔ It is possible

✔ not to prescribe benzodiazepine
✔ to prescribe benzodiazepine only for a few weeks
✔ To stop a long term benzodiazepine prescription

✔ How?
A LOT OF PROBLEMS IN THE WORLD WOULD DISAPPEAR IF WE TALK TO EACH OTHER