

IS THERE A RECREATIONAL MISUSE POTENTIAL FOR PREGABALIN? ANALYSIS OF ANECDOTAL ONLINE REPORTS IN COMPARISON WITH RELATED GABAPENTIN AND CLONAZEPAM DATA

FABRIZIO SCHIFANO¹, STEFANO D'OFFIZI^{1,2}, MICHELE PICCIONE², ORNELLA CORAZZA^{1,3}, PAOLO DELUCA³, ZOE DAVEY³, GIUDITTA DI MELCHIORRE¹, LUCIA DI FURIA⁴, MAGI' FARRE⁵, LIV FLESLAND⁶, MIIA MANNONEN⁷, AINO MAJAVA⁷, STEFANIA PAGANI⁴, TEUVO PELTONIEMI⁷, HOLGER SIEMANN⁸, ARVID SKUTLE⁶, MARTA TORRENS⁵, CINZIA PEZZOLESI¹, PEER VAN DER KREEFT⁹, NORBERT SCHERBAUM⁸

¹ 'ReDNet' and 'Psychonaut Web Mapping' Projects; University of Hertfordshire School of Pharmacy, Hatfield, UK

² Psychiatry and Clinical Psychology Department, Umberto I, "La Sapienza" University of Rome Medical School, Rome, Italy; Viale Regina Elena 244, 00161, Rome, Italy; doffizi.stefano@gmail.com; michele.piccione@uniroma1.it

³ Psychonaut Web Mapping Project; National Addiction Centre, Institute of Psychiatry, King's College London, London, UK; 4 Windsor Walk; SE5 8AF; paolo.deluca@kcl.ac.uk; zoe.davey@kcl.ac.uk

⁴ Psychonaut Web Mapping Project; Servizio Salute Regione Marche, Ancona, Italy; Assessorato Salute Regione Marche. Address. Via Gentile da Fabriano 3. Ancona 60100; lucia.difuria@regione.marche.it; stefy.pagani@gmail.com

⁵ Psychonaut Web Mapping Project; IAPS-IMIM-Hospital del Mar-UAB, Barcelona, Spain; Passeig Marítim 25-29. Barcelona 08003; MTorrens@imim.es; Mfarre@imim.es

⁶ Psychonaut Web Mapping Project; Bergen Clinics Foundation, Centre of Competence, Bergen, Norway; Vestre Torggate 11 - 5015 Bergen; arvid.skutle@bergenclinics.no; liv.holmefjord.flesland@bergenclinics.no

⁷ Psychonaut Web Mapping Project; A-Clinic Foundation, Department of Communications, Helsinki, Finland; Paasivuorenkatu 2A; 00530; Helsinki; teuvo.peltoniemi@a-klinikka.fi; aino.majava@a-klinikka.fi; miia.mannonen@a-klinikka.fi

⁸ Psychonaut Web Mapping Project; Addiction Research Group at the Department of Psychiatry and Psychotherapy, LVR-Hospital Essen, Hospital of the University Duisburg-Essen, Germany; Virchowstraße 174. D-45122 Essen; norbert.scherbaum@uni-due.de; holger.siemann@lvr.de

⁹ Psychonaut Web Mapping Project; De Sleutel Technische Bedrijfsseenheid Provinciale Staat der Broeders van Liefde, Merelbeke, Jozef Guislainstraat 43 a; B-9000; Gent Belgium; peer.van.der.kreeft@fracarita.org

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Corresponding author:

Professor Fabrizio Schifano
Chair in Clinical Pharmacology and Therapeutics
Associate Dean, Postgraduate Medical School
Consultant Psychiatrist (Addictions)
University of Hertfordshire
School of Pharmacy
College Lane Campus
Hatfield, Herts
AL10 9AB (UK)
telephone: +44 (0)1707-286107
fax: +44 (0)1707-284506
mobile: +44 (0)778 900 6809
email: F.Schifano@herts.ac.uk

ABSTRACT

Background: Although pregabalin abuse potential is reportedly low, online data related to its recreational misuse potential have recently been identified. We aimed here at formally analysing pregabalin misuse web reports and comparing these with data pertaining to similar drugs, e.g. gabapentin and clonazepam, for which an abuse potential has already been identified.

Methods: An 8-language analysis of the online information on pregabalin acquisition/misuse was carried out. An initial sample of 203 websites was considered and 108 relevant websites were monitored on a regular basis. To obtain material relating to gabapentin and clonazepam, an English-language search was carried out and 32 relevant websites were examined.

Results: Misuse of pregabalin, which is commonly offered for sale online, was allegedly associated with sedative and/or psychedelic effects. This was associated with both higher dosages than clinically advised and idiosyncratic (i.e.: IV, rectal, intranasal) drug intake modalities. Although perceived as less powerful than pregabalin, gabapentin misuse was associated with similar sedative/psychedelic effects. Clonazepam allegedly induced either sedation or stimulation, depending on the dosage.

Conclusions: Pregabalin experimenters might be profiled as individuals with a history of recreational polydrug misuse. Pregabalin misuse might be facilitated by easy online accessibility; potency; and peculiar, including anxiolytic, psychoactive effects. Physicians should carefully evaluate patients for history of drug abuse and observe them for signs of pregabalin/gabapentin/clonazepam misuse.

Key words: pregabalin, gabapentin, clonazepam, recreational use, Psychonaut Project, ReDNet project, online pharmacies, Internet monitoring

Introduction

With online pharmacies, prescription drugs may be more widely accessible (1-3). In particular, preliminary online information pertaining to both pregabalin purchase availability and its recreational misuse potential has been recently identified (4). Pregabalin is a prescription drug licensed to treat generalized anxiety disorder; partial epilepsy; and neuropathic pain. Since its misuse potential is reportedly low (5-7), we aimed here at formally analysing both pregabalin misuse anecdotal online reports and its online purchase availability levels. Pregabalin data were here compared with related clonazepam and gabapentin online information. In fact, pregabalin is structurally related to gabapentin (8), and shares some therapeutic indications with clonazepam. Interestingly, both clonazepam (9-11) and gabapentin (12-13) possess an identified abuse potential, at least in selected populations.

Materials and methods

Between January 2008 and August 2010, qualitative Google searches of 203 websites have been carried out in 8 European languages (English, German, Spanish, Italian, Dutch, Norwegian, Finnish, Swedish) using keywords such as 'legal highs'; 'research chemicals'; 'online pharmacy'; 'Lyrica'; 'pregabalin'; and 'online pharmacies'. Out of these, 108 websites were monitored on a regular basis, i.e. daily (n=21), weekly (n=32), monthly (n=55), depending on relevance; the remaining 95 websites were not considered here to be relevant. To obtain material relating to gabapentin and clonazepam, the Google search was carried out in English, with 52 websites examined and 32 identified as relevant. Links from above websites/forums, and other related material were followed as well. The SW London/St George's Ethics Committee granted the study permission.

Results

Pregabalin was here described as an 'ideal psychotropic drug' for recreational purposes to achieve specific mindsets, including: alcohol/GHB/benzodiazepine-like effects mixed with euphoria; to achieve entactogenic feelings and DXM-like disassociation; and to cope with opiates/opioids' withdrawal (Table 1). A pregabalin vs gabapentin experimentation YouTube video (14) was here identified as well. Misuse of pregabalin mostly seemed to occur orally, but IV; rectal ('plugging'); and 'parachuting' (emptying the content of the capsule into a pouch) self-administration techniques were also reported. Time of onset of the effects ranged here between 10mins-2hours, depending on the route of administration. Tolerance may reportedly develop fairly rapidly, to wear off quickly after drug cessation.

Similarly, gabapentin seemed to possess both heavy sedative ('..it's like I'm on a fully-sedated opiate buzz...') and psychedelic ('..I feel a disassociation much like DXM...'; '...1200mgs+ has me in an off buzz slightly reminiscent of MDMA...') effects. Interestingly, however, one user argued that 'pregabalin outshines gabapentin. Far less dosage to achieve the same recreational high...'. Similarly to pregabalin, drug tolerance could reportedly develop very rapidly.

Conversely, clonazepam was reportedly inducing either sedation (at 1-2 mg) or stimulation (at more than 8 mg). Clonazepam was typically co-administered with different sedatives and/or psychedelics. Pregabalin, gabapentin and clonazepam were commonly offered for sale on the web, without the need of a prescription.

Table 1: Summary of online alleged users' accounts of pregabalin, gabapentin and clonazepam misuse

Comments on dosages taken and the allegedly achieved psychoactive effects	According to pregabalin (mis)users, different dosages are associated with a vast range of effects:600mg : stumbling, disorientation, increased physic and psychological awareness, difficulty to drive, slurred and broken speech, hearing and visual alterations/hallucinations, double and blurred vision, uninhibited behaviours, talkativeness, increased body energy, increased sexual performances. 900mg : strong feelings of drunkenness, difficulty to walk, alteration of colours perception, little euphoria. 1200mg : drowsiness, euphoria, entactogenetic feelings. >1500mg (to 5 g) : uncontrollable drowsiness, frequent hallucinations, great euphoria, frequent dissociative events (described like dextromethorphan/DXM-like dissociative effects), behavioural inhibition, anxiety, and necessity to move..." (15) "I am interested in using it to combat heroin withdrawals" (16) ".....the pregabalin erases my benzo, opiate withdrawal and cravings... IMO anything over 900 mg is a
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	<p>waste - too sedating." (17)</p> <p>"SWIDr has tried Pregabalin .. He seemed very relaxed (anxiety free), not too much euphoria but some, DXM dissociative-like effects...." (15)</p> <p>"Yes, it is similar to a benzo high.....I would say it is more similar to GHB..." (16)</p> <p>Gabapentin "...The most I have done has been 4800mg of the 600mg pills whilst the lowest amount that I can take to get any effect seems to be around 900mg or more.... To classify this pharm is a near impossible task. It is everything and anything in one pill. The only downside to gabapentin so far as I can tell, is the onset. These little guys take upwards of an hour to really start to kick in, but luckily, they last for 4-8 hours it seems..... I feel as if I'm on a super amphetamine rush and can tackle anything, yet feel so content it's like I'm on a fully-sedated opiate buzz. I'm chatty and witty, deep and insightful...." (18)</p> <p>".. I knew that I need at least 10 300's to get the right effect. Most everyone else I know that takes gapapentin take only 7 or 8... so about an hour taking after them I feel a disassociation much like DXM, but only in my head and hands. My worries started to fade away. I am a very quiet, shy person normally, but when I am on gabapentin after about 1.5 hours I get very friendly, very talkative, very active, very uninhibited... You really need to walk around on gabapentin dancing would be incredible..." (19)</p> <p>".....The feeling was comparable to cannabis with more of a heavy feeling in the body...." (20)</p> <p>Pregabalin vs gabapentin recreational psychoactive effects "...In my opinion, pregabalin outshines gabapentin. Far less dosage to achieve the same recreational high. Also not as strong of a half life allowing one to use the drug more frequently (ie. every weekend)...." (20)</p> <p>Clonazepam Most reports suggest 1-2 mg to achieve sedation; euphoria is achieved by increasing the dose to 8-12 mg; "... About 10 minutes after insufflation, I noticed a high or buzz much like that I remember when I was being sedated before dental surgery. It was very pleasant, and I felt very relaxed...." (21)</p> <p>"At first I felt a bit disorientated, some kind of anguish were crawling under my skin almost as I feel when I have smoked alot of pot." (Zazaz, 2008; Erowid)</p>
<p>Different routes of administration</p>	<p>Pregabalin <i>Intravenous</i> "When the effects wore off, I decided to shoot one capsule. That was fantastic, I felt so good!! Now I will only use the lycra IV. (it is perfect for injection, you empty the capsule in the cup.....you shoot a very pure solution)" (17)</p> <p>"I tried injecting it also. Almost all the powder inside the capsule is not water-soluble, but the pregabalin is very water soluble, so with a big cotton I was able to get a pretty damn clear solution outta there...." (16).</p> <p><i>Rectal/plugging</i> "SWIM (a 75kg male) ... put the contents of a 75mg pregabalin capsule into water, and it didn't dissolve (which seems odd that pregabalin should be freely water soluble, but maybe more water would have been needed to dissolve all powder), but SWIM plugged the mixture....Effects were felt after 5 minutes, were very close to the peak at 10 minutes, and did peak at 15 minutes. The effects seemed a bit more relaxing than usual, and it is hard to judge but SWIM would say that it shared a duration with oral administration and this dosage is equivalent to 150-300mg taken orally...." (15).</p> <p>"Swims used the drug rectallynotices that its alot more soluble when the cap is opened first and the powder emptied out but if you dont want to go through the hassle hot water will easily dissolve the whole capsules. Just let it cool down a little before plugging." (15).</p> <p><i>Parachuting</i> "I just parachuted 2000 mgs of pregabalin powder. In two hours I'll see how f....d up I am. I have huge tolerance though..." (17)</p> <p>Gabapentin: oral; intramuscular</p> <p>Clonazepam: oral; crushed and eaten; snorting (grinding up the tablet and snort the mixture); intramuscular</p>
<p>Tolerance</p>	<p>Pregabalin "Lyrica has an extremely high ceiling. I'm not suggesting you do 600+mg your first time, but I have taken amounts 3000+mgs[...] with Lyrica you gain tolerance extremely quickly." (17).</p> <p>Gabapentin "..The most troubling thing about gapapentin was the tolerance level was very high. Each successive</p>

	<p>dosing required more and more to achieve the same level. Doing gabapentin two days in a row was impossible...." (20)</p> <p>Clonazepam "...The benzo (clonazepam) created a very creative and almost 'giddy' type of reaction similar to most other benzodiazepines, except this time at a much lower dose and on a much more enjoyable level (especially considering my tolerance)..." (21)</p>
Use in combination with other substances	<p>Pregabalin is reportedly often taken in combination with other compounds in order to potentiate their effects, such as (4):</p> <ul style="list-style-type: none"> • Alcohol • Prescribing drugs: benzodiazepines; zopiclone; gabapentin • Illicit/recreational drugs: hashish/marijuana; heroin/opiates; amphetamines; LSD. • 'Legal highs': mephedrone/'meow meow'; Salvia divinorum <p>Gabapentin: "...I love Gabapentin especially with Baclofen. 600-900mgs gives me a nice happy feeling, 1200mgs+ has me in an off buzz slightly reminiscent of MDMA..." (23). Other drugs reportedly taken in combination with gabapentin include: cannabis; alcohol; SSRIs; LSD; amphetamine; GHB.</p> <p>Clonazepam: Psychoactive drugs reportedly taken in combination include: mushrooms; MDMA; 2C-T-2; cannabis; nitrous oxide (24); alcohol; morning glory seeds (25)</p>
Illustrative examples of websites allegedly offering pregabalin/gabapentin/clonazepam for purchase (as of August 2010)	<p>Pregabalin http://www.drugshoponline.com http://www.medrex-one.com http://www.ipharmacylist.com https://www.israelpharm.com http://www.canadadrugsonline.com http://www.medsupport.org http://www.eurodrugstore.eu http://www.easy.md</p> <p>Gabapentin http://www.pharmacyescrow.com/s4515-s-NEURONTIN.aspx http://www.77canadapharmacy.com/gabapentin.php http://www.omfgg.com/profiles/blogs/order-gabapentin-online-order http://firsthealthstore.net/products/neurontin.htm</p> <p>Clonazepam http://www.generictab.com http://www.buy-clonazepam.com http://www.coryholt.com http://www.elegantinteriorsanddesign.com</p>

Legenda: IMO: in my opinion; SWIM: somebody who is not me; DXM: dextromethorphan. Please note that although spelling mistakes have not been edited, rude words have been deleted. Most data collected from online forums that could be seen as personal identifiable (e.g. usernames, complete URLs for specific threads etc) were here appropriately anonymised.

Discussion and Conclusions

Pregabalin experimenters might be profiled here as individuals with a history of recreational polydrug misuse (14; 26). Pregabalin dosages most typically reported were clearly in excess (e.g. up to 5g) of the maximum level (e.g. 600 mg; 27-28) which is clinically advisable. If pregabalin is perceived by misusers to be a valid substitute for most common illicit sedative drugs, this may be a reason for concern.

One could wonder about the anxiolytic properties of pregabalin, gabapentin and clonazepam as potential mediators for misuse. In fact, some users might start self administering with these GABA-ergic drugs as a way of self medicating. Because of rapid development of high tolerance levels with both pregabalin and gabapentin, then increasing dosages are self-administered. Consistently with this self medication hypothesis, some users advised either on the concurrent administration of pregabalin with gabapentin, or on their association with other sedatives, such as alcohol, benzodiazepines and zopiclone.

In line with observations here presented, pregabalin is indeed characterized by higher (2.5 times; 29) potency; quicker absorption rates and greater bioavailability levels than gabapentin (30). One could wonder why both gabapentin and pregabalin, in apparent contrast with clonazepam, seem to possess both a sedative and a dissociative effect as well. Although all three compounds are GABA-ergic, pregabalin (31) and gabapentin (8; 32) precise mechanism of action is still unclear. Conversely, clonazepam is a well characterized, powerful compound

which seem to have replaced flunitrazepam as the most popular misusing benzodiazepine (10). A better clarification of the pregabalin misuse potential level is of interest, since the drug has recently been proposed as a treatment for substance misuse, namely for both alcohol (33) and benzodiazepine dependent (34) individuals. Pregabalin potential of misuse is not typically mentioned in the prescribers' aides (e.g. 27; 35). However, controlled clinical studies carried out in over 5500 patients have shown that in some patient populations self-reporting rates of euphoria ranged between 1 and 12% (29). Abrupt/rapid discontinuation of pregabalin may be associated with insomnia, nausea, headache, or diarrhoea, which may be suggestive of physical dependence (36-37).

One could wonder about the limitations of carrying out a risk of misuse assessment of a drug whilst taking into account the online comments only. In fact, it may be inappropriate to trust information obtained from the internet without independent verification. In April 2010, however, pregabalin has been included in the list of new recreational psychoactive substances officially notified to the relevant EU agencies (38). These concerns have recently been confirmed through analysis of the adverse drug reactions' Swedish national register data (39). Finally, pregabalin is a controlled substance under Schedule V of the United States' Controlled Substances Act.

One could think that only large scale, adequately controlled, clinical studies can give a clear indication of drug characteristics and adverse effects. However, in line with present observations, previous studies from our group (40-41) have clearly suggested that increase in online trafficking/debate about a specific psychoactive drug typically precedes the occurrence of clinical incidents at the population level. As with any centrally active drug, physicians should carefully evaluate patients for history of drug abuse and observe them for signs of anticonvulsants', including pregabalin, misuse (37; 42).

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