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ORIGINAL ARTICLE

The use of ketamine to cope with depression and post-traumatic stress disorder: A qualitative analysis of the discourses posted on a popular online forum

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ABSTRACT

Background: Because of the shortcomings of traditional pharmacotherapy for major depressive disorder and post-traumatic stress disorder (PTSD), there has been growing interest in the rapid mood-enhancing effect of ketamine.
Objectives: To analyze what has been posted about ketamine use for dealing with self-reported depression and/or PTSD on one of the biggest international message boards on the internet.
Methods: Qualitative study with online observation of threaded discussions on Bluelight. In-depth online searches were conducted in 2018. Twenty-nine threads, with a total of 708 units of analysis, were selected and subjected to content analysis, where, via a coding process, the units of analysis were organized into nodes.
Results: Despite having several negative effects (e.g. dizziness, nausea and inability to talk), the examined discourses suggested that the use of ketamine to elevate mood was both efficient and worthwhile. Intranasal use was the most common route of administration mentioned. We traced how the mood enhancement caused by ketamine is perceived: the loss of pleasure disappears, as well as the depressed mood; the markedly diminished interest in activities vanishes and motivation comes back. From all the posts analyzed, only two reported negative outcomes (i.e. no mood-enhancing effect). The most mentioned adverse event was damage to the urinary bladder and the kidneys in cases of misuse.
Conclusion: Although online research of user-generated content has its limitations in terms of reliability and validity, the present study adds relevant information on the use of ketamine for managing depression and PTSD, whether this use is done legally or not.

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Introduction

Major depressive disorder (MDD) is the most common psychiatric disorder in developed countries (1,2). Post-traumatic stress disorder (PTSD) is also a complicated issue in psychiatry (3,4). MDD co-occurs in most individuals with PTSD, and the co-occurrence of these disorders is associated with a more severe clinical presentation compared to either disorder alone (5,6).

The attainment of remission (i.e. the reduction of symptoms/scores to a minimal absolute level) in both disorders is a challenge because current pharmacological treatment options take two weeks or more to induce a therapeutic response (i.e. a clinically significant improvement, typically operationalized as 50% reduction in whatever scale is being used) (7,8). This latency period significantly increases risk of suicide and self-harm and is a key public health issue (9). The low rates of efficacy add to the limitations of the current depression therapies (10): only one third of depressed patients remit during their first antidepressant treatment (8,11,12). Moreover, after having followed all the available treatment options, including electroconvulsive therapy (ECT), around 20% still have disabling symptoms, constituting a group with treatment-resistant depression (TRD). Similarly, antidepressant pharmacotherapy for PTSD is associated with high rates of residual PTSD symptoms. According to Albott et al. (2018), this information attests to the inadequacy of standard antidepressant pharmacotherapy as a treatment for many individuals living with PTSD and MDD, let alone for individuals with the more complex and severe comorbid presentation (13). Antidepressants are helpful in managing PTSD symptoms, such as loss of interest or pleasure, irritable mood, sadness and anxiety (13,14). A meta-analysis

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performed by Rytwinski et al. (2013) analyzed 57 studies (n = 6,670 participants). It revealed that 52% of individuals (95% confidence interval) with PTSD had co-occuring MDD (6). Shalev et al. (1998), in a prospective study about PTSD and depression following trauma with 211 trauma survivors, have found that comorbid depression occurred in 44.5% of patients with PTSD at one month after the traumatic event and in 43.2% at four months; this comorbidity was associated with greater symptom severity and lower levels of functioning (15).

Because of the shortcomings of conventional antidepressants, there has been growing interest in the rapid mood-enhancing effect of ketamine (9,13), which is best known as an anesthetic medication and as a recreational drug. It has been shown to reduce depressive symptoms and even suicidal ideation within hours (10,16–24). The fast antidepressant effect of ketamine is considered one of the biggest breakthroughs in the treatment of depression in recent years (10,21).

Several studies have demonstrated that intravenous (IV) ketamine can induce an antidepressant effect in patients with depression who were previously resistant to standard treatment with oral antidepressants as well as ECT (17,21,25–31). Ketamine's possible antidepressant effect has been described to last from three days to a few months, with a median relapse time of eighteen days (25,32). However, the study that showed the highest inter-individual variability in duration of response (32) applied an open-label design. Therefore, longer term placebo-controlled studies are needed to test this approach further. Antidepressant effects of ketamine occur at subanaesthetic doses, as these are the doses that have mainly been studied (33–37).

Ketamine seems to have a wide range of potential applications in psychiatry. Besides the aforementioned ones, ketamine has shown interesting results in the treatment of alcohol dependence. Subanaesthetic doses of ketamine are not rewarding (38), and some studies have shown that recently detoxified alcoholics given ketamine did not go back to their alcohol consumption (39,40). Also, for cocaine dependence, ketamine seems to produce positive results. Dakwar et al. (2019) reported that a single ketamine infusion in 55 cocaine-dependent individuals, coupled with a mindfulness behavioral modification programme, promoted abstinence and reduced the risk of relapse. It also suggests that ketamine may help patients gain more benefit from behavioral interventions by reducing cravings, increasing motivation, and dampening reactivity to high-risk situations (41).

One new way to gain more information about ketamine use, especially with respect to the patients' perspective, is to turn to drug-related forums on the internet. Those cyber communities are increasingly used to provide information regarding safety, harm reduction, and general facts about drugs, to share advice on optimal drug use, and to discuss about popular choices and experiences (42,43). This makes the internet the most popular source of information on drugs and their use for the general public (44).

Therefore, monitoring drug-related internet forums, where drug users describe their experiences, is potentially important to identify and understand new trends (43,45). The topic of licit and illicit drug misuse is well-suited to internet-based discussion, with its relative anonymity and apparent freedom from real-world constraints, including geographic and legal boundaries, facilitating access to a hard-to-reach population (43). Online forums can create new pseudo-individual and group identities by channeling physical and social experiences, establishing psychological connections between members and offering opportunity for social advancement (42). It has been observed that those self-constructed virtual communities constitute a place where individuals sharing interests in similar, albeit unconventional topics, can establish a broad, self-renewing and up-to-date network, which might not otherwise have been possible (43).

On online drug forums, there are threads not only for discussing recreational drug use, but also threads dedicated to the use of psychoactive drugs for dealing with mental disorders, such as depression and PTSD. People may use these sites to discuss different aspects of their disorder, including personal experiences with treatment and coping with the disorder. Thus, these forums may provide additional information on important still-unanswered questions about the patients' perspective on optimal dosage, route of administration, treatment duration, as well as negative effects and addictive properties of ketamine.

The present study aims to identify and analyze what has been posted about ketamine use for dealing with self-reported depressive symptoms on one of the biggest international drug fora on the internet, the Bluelight website.

Methods

Ethics

The Ethics Committee of the *Universidade Federal de São Paulo* (UNIFESP) has approved the project (protocol number 2.408.023).

The ethics committee statement and other required documents were sent to the Bluelight administrators. This procedure complies with the best practice protocols for online research (42,46–49) and the research guidelines from Bluelight (50). Because all messages on Bluelight become the exclusive property of the

website administrators, we required and obtained consent to use the data published on Bluelight, as well as the permission to mention the website in this article.

To post a message in any forum on Bluelight, it is necessary to subscribe to it, which denotes an expectation of privacy by having membership policies and not accepting unknown members (43). To maintain privacy, threads and users' names and URLs have been anonymized in this article.

Data collection

We designed a qualitative study to extract and evaluate threaded discussions on Bluelight (www.bluelight.org), one of the main websites with user generated content about drugs, drug use and harm reduction. Bluelight has been online for more than 20 years and hosts between 7,000 to 10,000 users per month (51).

The internet discussions assessed in this study included descriptions of regimens used for relieving depressive and/or PTSD symptoms with ketamine, all of which had its content presented in English. The term "thread" refers to a file with a specific threaded discussion. Each thread is constituted by posts, i.e. messages/comments posted by the Bluelight community. Every Bluelight member can open a thread and the whole community can reply to it. Bluelight has a team of moderators to avoid drug trading, violent speech, and improve communication between staff and members.

Data collection followed two steps (1): Using Bluelight's search tool, threads with the terms [ketamine AND depression], [ketamine AND post-traumatic stress disorder] and [ketamine AND PTSD] in its content were investigated (2). Threads with explicit reference to the use of ketamine for relieving self-perceived depressive and/or PTSD symptoms were selected. This is important to remark because several threads are opened in order to discuss a scientific article, for example. This was not our focus. The goal was to trace personal descriptions about the use of ketamine and its effects in managing self-reported depressive and/or PTSD symptoms. So, threads with a personal experience in its opening post were selected. Sixty-three threads were excluded (22 threads with the initial post regarding scientific articles, 38 threads with a question as the opening post, and three threads where the initial posts were complete reviews about ketamine made by the Bluelight community. In total, 29 threads (T1-T29) were selected.

Qualitative in-depth online searches were conducted in October 2018 in order to collect data. The selected threads for data analysis have posts dating from April 2008 until October 2018. An unobtrusive observational approach was taken, i.e. the threads were viewed, but no posts or other contributions to private or public discussions were made, and no information or clarification of content was sought by any members of the research team (43).

Data analysis

Data analysis, coding, and interpretation of the selected threads were performed by two of the authors. Inter-rater reliability was checked through overlapping the results obtained by these two authors and discussing them extensively; discrepancies were solved through consensus.

All selected threads were subjected to a thematic content analysis (52–54). Data were collected by printing and archiving the whole thread.

On Bluelight, every post made in a thread is identified with the name of the person who wrote the post (usually an avatar, i.e. an icon or figure representing a particular person in a video game or internet forum), date and time of publication. Every post made in the selected threads passed through content analysis. Consequently, the units of analysis of this study are every individual post made in the selected threads. A total of 708 posts were analyzed.

The content analysis was performed with the support of the software NVivo 12 (QSR, Melbourne, Australia). It helped with the coding process, where the units of analysis were separated into nodes (i.e. a collection of references about a specific theme). The relevant themes for this study were: (1) reasons for using ketamine, (2) positive and (3) negative effects, (4) ketamine use regimen (dose, route of administration, frequency of use), (5) safety, (6) interaction with other substances, (7) addiction and (8) suicidal ideation. These themes were developed accordingly to our doubts about different ketamine regimens being applied all over the world. We were attentive to the emergence of new themes during data analysis, which did not happen. Thus, we kept the themes as initially organized.

Each node was then isolated, making it possible to analyze what was posted about each theme across all selected threads. For example, the node "addiction" contained all the posts about this theme, from all chosen threads. The corresponding node was then evaluated in the triangulation and categorization processes, which allowed the recognition of patterns in the selected discourses (53,55).

Along this article, the reports are followed by a code that identifies the source of the report. Threads are named "T1" for "thread 1", "T2" for "thread 2", and so on. The term "members" is used to refer to the people who contributed to the development of the analyzed threads.

Results

Table 1 gives an overview of each thread (number of posts, number of members and themes mentioned in each thread).

Table 2 provides an illustrative quote from each theme analyzed.

Reasons for using ketamine: coping with depressive symptoms and suicidal ideation

Whether the members are legitimately suffering from MDD, with an official diagnosis given by a health care professional and fulfilling the diagnostic criteria for such a condition, is not possible to determine. Their self-perceived depression and/or PTSD are considered sufficiently valid for the purposes of this study.

According to the DSM-5 (2013), the most remarkable symptoms of MDD are depressed mood (with subjective reports of sadness and hopelessness considered) and loss of interest or pleasure (56). These traits are described in the analyzed reports. The treatment-resistant aspect of depression was reported with great sorrow: *"I don't care who you are – depression will eat your heart, soul, and mind alive"* (T1). In this scenario, using ketamine is seen as another attempt to have a regular life (see Q1, in Table 3).

Members usually share their experiences with other drugs, mainly with prescribed antidepressants and psychedelic drugs. According to several posts, conventional pharmacotherapy had no effect in treating their self-reported depression (see Q2 and Q3). Ketamine appears as an alternative not only for oral antidepressants, but also for ECT, a treatment that several members want to avoid (see Q4 and Q5).

Additionally, some members consider ketamine a useful tool for suicidal ideation because it provides immediate relief (see Q6). In this sense, ketamine is described as a real *"lifesaver"* (T6) (see Q7).

Table 1. Overview of the analyzed bluelight threads.

Thread	Number of posts (units of analysis)	Number of members	Themes mentioned*
T1	139	51	All
T2	13	9	2, 3, 4, 7, 8
T3	59	19	1, 2, 3, 4, 7, 8
T4	8	3	4
T5	13	6	All
T6	112	65	All
T7	7	6	2, 4
T8	6	5	2, 4, 7
T9	36	18	4, 5, 7
T10	4	3	2, 4, 6
T11	10	6	2, 3, 4, 5
T12	11	5	2, 3, 4, 8
T13	4	3	1, 2, 4
T14	13	7	4, 6
T15	4	4	1, 2
T16	21	13	1, 3, 4, 7
T17	43	18	2, 3, 4, 6, 8
T18	3	2	1
T19	41	17	1, 2, 3, 4, 7, 8
T20	15	7	3, 4, 6
T21	32	19	1, 2, 3, 4, 7, 8
T22	14	7	4, 6
T23	6	3	4
T24	11	8	1, 2, 3, 4, 6
T25	11	10	1, 4, 7
T26	10	5	1, 4, 6
T27	5	5	1, 2, 4
T28	24	10	1, 2, 3, 4, 5, 6
T29	33	15	1, 3, 4, 5, 7

* 1 – reasons for using ketamine, 2 – positive effects, 3 – negative effects, 4 – ketamine regimen, 5 – safety, 6 – interaction with other substances, 7 – addiction, 8 – suicidal ideation.

Table 2. Illustrative quotes from each theme.

THEMES	ILLUSTRATIVE QUOTES
1. Reasons for using ketamine	*"I sometimes get terribly depressed in the winter time […] and I am uncomfortable about taking mainstream pharmaceuticals for winter blues […] I've done many, many different natural regimens and they're mostly temporary. I need to try something a little less conventional."* (T21*)
2. Positive effects	*"My mood brightened (beyond mere dissociation) after ~7 hours […] I just noticed while walking around outside that I just felt 'ok' and 'kind of optimistic'. I stopped dosing after 3 days. My mood remained similarly bright for about 2 weeks."* (T21)
3. Negative effects	*"As for long term use though, some people (myself included) cannot consume the 5 × 40 mg a day mentioned somewhere in this thread, as after a week I start to get unpleasant sensations from my lower abdomen, which rapidly proceeds to excrutiating pain if I continue to use."* (T6)
4. Ketamine regimen	*"I've recently been started on oral ketamine troches for treatment resistant depression and anxiety. 150 mg at the moment which I have been taking orally (green gummies) […] I am finding that this ROA* [route of administration] *is ridiculously low compared to IM, nasal and IV."* (T22)
5. Safety	*"I haven't heard of any deaths by K OD* [ketamine overdose], *only things like hyperventilation from mixing K with depressants."* (T28)
6. Interaction with other substances	*"Based on a T6 writeup, I started taking hydergine* [gabapentin] *at day one. This was a mistake. It potentiated the side effects of the* [ketamine] *regimen too strongly."* (T1)
7. Addiction	*"The addiction potential to ketamine is high, especially, I'm pretty sure, with the frequency you'd need to do it to keep the* [mood-enhancing] *effects consistent […] It seems that the key to success is to avoid abuse and treat it as a medicine instead of getting high."* (T21)
8. Suicidal ideation	*"Nothing was looking good and I was probably for the first time really considering on ending it all. So there I am, fetal position in the shower, crying like a baby. Decide to do I believe 250 mg* [of ketamine]. *I started looking at all the good things that I was over-looking."* (T21)

* T = thread

Post-traumatic stress disorder

Frequently, a traumatic event was the cause of their depression and some members mentioned having PTSD (see Q8). Also, in these cases, ketamine seemed to work (see Q9).

Interestingly, a T27 member connected his/her PTSD symptoms to a social phenomenon that traumatized a considerable amount of people at the same time: ASS – AIDS survivor syndrome (see Q10), a collective trauma caused by the spread of HIV in the 80's and 90's. The experience with ASS can help us to overcome the also traumatic consequences caused by the covid-19 crisis.

PTSD was not the only comorbid disease mentioned. Other members also reported experiencing disabling anxiety. Chronic pain was frequently mentioned, too.

Positive effects

Several members reported having discovered the mood-enhancing effect of ketamine with recreational use (see Q11). A T17 member realized that his/her depression was *"totally gone"* after having ketamine as anesthesia for a spinal surgery.

Members stated that ketamine *"re-wires"* the brain and enables it *"to deal with how shitty real life is"* (T1). A T28 member felt like *"the reset button has been pushed"* on his/her brain. Therefore, ketamine would not be just a temporary fix to depression, but a real *"opportunity for you to explore the root of it"* (T1). On the other hand, some members describe the mood-enhancing effect of ketamine as a quick short-lasting management tool (see Q12).

In the subjectivity of their discourses is possible to trace how they perceive the mood enhancement caused by ketamine. The loss of pleasure disappears, as well as the depressed mood (see Q13 and Q14). The markedly diminished interest in activities (another diagnostic criterion for MDD according to the DSM-5) vanishes and motivation comes back (see Q15).

Anxious distress can co-occur with MDD (56) (see Q16). Also considered a diagnostic criterion for MDD, the diminished ability to think or concentrate, or indecisiveness, can be dissipated by ketamine (see Q17).

Two posts (i.e. two units of analysis) address having no mood-enhancing effect after using ketamine (see Q18 and Q19).

The analyzed posts describe ketamine's afterglow duration as variable (one week to three months), but one thing is solid in their discourse: ketamine is effective in decreasing the self-reported depressive symptoms and has been an important tool for the studied Bluelight members to overcome depression or PTSD, even for a short period of time, which is reported with great relief.

Ketamine regimens: focus on routes of administration and safety

Intravenous ketamine use is acceptable in a medical setting, according to the analyzed reports. *"IVing is out of question, and I can only call it abuse"*, says a T6 member about self-administering ketamine intravenously. The intravenous route was mainly reported by those who took part in a clinical trial or were under treatment in a ketamine clinic, i.e. by those using ketamine in a medically assisted environment. The intramuscular route is mentioned as a good alternative to intravenous administration, but the perceived risks, such as getting infected, make it unpopular in the studied group.

Despite the ease of administration, taking ketamine orally is described as a waste in managing depressive symptoms, because of its low bioavailability through this route. Not only a waste, but also dangerous. A T19 member warns for the danger of using the oral route (see Q20). Nonetheless, some members reported using oral ketamine as lozenges (T3) or gummies (T22) produced by local pharmacies, and described the elevated mood feeling as ephemeral.

The intranasal formulation of ketamine appears as a good alternative. It is the most frequently mentioned route of administration, with the drug being obtained either legally or illegally. Legally, it has been prescribed as an intranasal spray and produced by local pharmacies, even before the pharmaceutical company Janssen obtained its esketamine nasal solution approved by the United States Food and Drug Administration (FDA), in 2019.

For the members who obtain ketamine illegally, the best results are obtained with the intranasal route. For members using ketamine in a medical setting (i.e. ketamine clinic or clinical trial), the IV and IM routes are considered very effective. Interestingly, different routes can be combined in a treatment protocol. For instance, a T10 member receives IM ketamine infusion in a clinic, followed by a prescribed intranasal spray that should be used as needed. Other routes of administration mentioned were: inhalers (T17), nebulizers (T17), suppositories (T10) and subcutaneous (T1).

Ketamine's safety as an anesthetic was debated (see Q21), as a way to back up the security of their own use of ketamine. The real danger was seen in feeling depressed (see Q22). Members do not want to go back to depression. And they say they do not need to, once they have experienced the mood elevation caused

Table 3. Results – quotes from the analyzed threads on Bluelight.

Q1	*"I've been depressed for over 20 years now. The last 6, I've spent in bed (literally) watching my husband and children do things I can only hope to do again. Please help."* (T18*)
Q2	*"I have suffered from depression for most of my life. After the 12th SSRI, it was clear that waiting another 8 weeks to feel nothing but worse wasn't going to work."* (T24)
Q3	*"I have treatment-resistant depression and have been treated without success for the last 30 years. I have taken every type of medication that is on the market with no long-term success."* (T14)
Q4	*"With the specter of ECT looming on the horizon, I'm looking into ketamine for treatment-resistant depression."* (T3)
Q5	*"Besides ketamine, the only option left was ECT (no, thanks, my memories are all I have)"* (T19), referring to a possible negative effect caused by ECT: memory loss.
Q6	*"I use it when I am like totally suicidal and can't do anything but stay in bed miserable […] Ketamine even at a tiny dose, once in the morning IM* [intramuscularly], *makes me happy all day"* (T6).
Q7	*"I honestly think if I wasn't able to do it* [ketamine] *at all, I'd just continue with my plans of suicide that I had for many years and long before I ever used ketamine"* (T6).
Q8	*"I have real reasons for needing a dissociative. Mental health is my reason. Childhood abuse […] and subsequent PTSD."* (T29)
Q9	*"It* [ketamine] *repaired the parts of my brain that experienced harm from repeated traumatic events."* (T1).
Q10	*"Many of us who survived the 80's and 90's lost scores of friends to HIV-related illnesses. Now we are 'of a certain age' and many of us, both HIV positive and negative, have been experiencing symptoms that are similar to PTSD. […] ASS is for AIDS Survivor Syndrome. I've been suffering from sometimes disabling anxiety for the past 10–15 years."* (T27)
Q11	*"I anecdotally noticed being in a better mood after a brief stint of recreational ketamine use almost 10 years ago […]"* (T1).
Q12	*"Using ketamine seems more like a symptom treatment to me, but no doubt it can apparently be effective on short-term, yielding pretty much immediate benefit."* (T1).
Q13	*"[…] a pleasant state of balance that felt nice rather than dull, and that gave me an aura that seemed to make everyone feel attracted to me […]"* (T6)
Q14	*"I instantly went from being dark and gloomy with a side of suicide to bright and chipper dipper with a big smile and the will to live."* (T1)
Q15	*"I feel better. More motivated. The future isn't as dark."* (T2)
Q16	*"The effect I enjoy the most is complete freedom from the anxiety that constantly eats at me."* (T6).
Q17	*"[…] easier to observe alternative pathways of action and carry them out without hesitation […] lingering thoughts of past traumas that used to come up in the back of my mind are now quiet."* (T1)
Q18	*"I have access* [to ketamine] *and so forth, but it doesn't seem to serve my particular situation."* (T5)
Q19	*"I have undergone a lengthy series of ketamine treatments, including IV infusions in a hospital environment. Unfortunately, ketamine provided no improvement."* (T1)
Q20	*"[…] its* [ketamine's] *piss-poor oral bioavailability means that oral preparations are going to involve fairly high doses, which creates a major incentive for either snorting or injecting the drug to achieve euphoria or re-selling it on the black market."* (T19)
Q21	*"[…] as an anesthetic* [ketamine safety] *is established beyond all doubts by years of use on all kinds of animals, including human children."* (T6)
Q22	*"It* [ketamine] *definitely has its risks, but so does sitting around in a depressive episode with constant suicidal ideation."* (T1)
Q23	*"At first, I just fell in love with it* [intranasal ketamine] *and I abused it. I sucked the nasal spray into a syringe and IM'ed."* (T16)
Q24	*"Low dose ketamine worked for me. But it is always tempting to take more to go down the rabbit hole."* (T25)
Q25	*"I'm certain very few (if any) would be disciplined enough to resist falling into recreational doses and daily use* [of ketamine]." (T9)
Q26	*"This regimen is for those who embody the utmost self-discipline […] I only acquired 1 gram of pure ketamine, more than enough to last for one cycle of this regimen. Though I am not prone to addiction, the choice to not purchase more was a precautionary measure to prevent abuse. I advise anyone doing this procedure to do the same."* (T1)
Q27	*"Ketamine's euphoric and transcedent properties make it a substance easily abused. Even in a low-dose regimen, the temptation to do 'just a little more this dose' can be ever present. Each brief period of euphoria makes you feel as though you are close to a supreme truth, if only you could do just a little more to figure it out. Do not chase this feeling, it is a transient, false lure."* (T1)
Q28	*"[…] This* [low-dose binging] *regimen trains you to be fixated not only on doing ketamine constantly, but also to the idea of ketamine itself. […] in my opinion it would be better if people with any prior history of drug addiction should avoid trying this procedure entirely. In my experience, it has been safer and more effective to use dissociatives very rarely, once a month max."* (T6)
Q29	*"I actually really dislike the effects of ketamine, but I can survive an hour of discomfort if it means that I'm spared such a massive load of fatigue and depression throughout the rest of the week."* (T1)
Q30	*"[…] my depression had caused me to forget how love works. Ketamine has at least in part allowed me to remember it […]. I'd rather die than forget love again … "* (T6)
Q31	*"There was minor kidney colic."* (T1)
Q32	*"[…] unpleasant sensations from my lower abdomen, which rapidly proceeds to excruciating pain if I continue to use."* (T6)
Q33	*"I have absolutely no doubt that gabapentin works wonders to 'rekindle' the effect."* (T6)
Q34	*"[…] I have also found that using hydergine concurrently with the procedure tends to enhance the effects."* (T6)
Q35	*"Taking hydergine as per* [T6] *report did not pan out well for me […]. Some of the 'side effects' I was attributing to ketamine were in fact from hydergine, and once I removed it, the ketamine side effects were downgraded to being far less severe."* (T1)

* T = thread

by ketamine: *"I don't anticipate depression anymore, I just do the* [ketamine] *injection"* (T1).

Dealing with negative effects: misuse, addiction and harm reduction

With expanding popularity in the United States, prescribed nasal sprays of ketamine are convenient for ketamine treatments outside a medical setting; however, it brings a new way of misusing ketamine, as described by a T16 member (see Q23). Consequently, the intranasal formulation presents the same risk of oral formulations: they can lead to self-administration of higher doses than prescribed and the use of other routes of administration in order to potentiate the effect.

Ketamine causes rapid tolerance buildup, so even when microdosing, members reported walking a dangerous path (see Q24). The risk of falling into recreational use is ever present according to some members (see Q25).

Members consider addiction a major risk of ketamine use. Not surprisingly, the main disclaimer on the analyzed threads was about the risk of getting high

instead of keeping the doses low, which is enough for the nootropic and mood-enhancing effect of ketamine: *"Remember: the goal is to repair your brain, not to get high"* (T1).

Members appear experienced, sharing harm reduction strategies. They already know they will have dissociative sensations (i.e. out of body feelings) when they use ketamine, so they manage this effect, for example, using ketamine in their home with the mobile phone close to them, in case they need to call for help (T5), and with food supply, so they do not have to leave their home in any case (T1). Limiting the amount of ketamine available was also mentioned as a strategy to limit the consumption (see Q26). Having to control the cravings for a bigger dose was repeatedly warned by the threads that discussed the low-dose binging ketamine regimens (see Q27 and Q28).

Several negative effects were mentioned. Interestingly, dealing with them was not described as the biggest problem in their ketamine regimen. For instance, dizziness was not described as a negative effect, but as *"a natural part of the treatment"* (T2). Notably, these negative effects were not reported as a burden. Instead, coping with depression was described as the real burden in their lives (see Q29 and Q30).

Double vision (T17), hallucinations (T28), nausea (T1), and inability to talk (T17) were also characterized as negative effects. The urinary bladder and the kidneys were the most mentioned affected organs (see Q31 and Q32). Anxiety, insomnia and paranoia can also occur, even with low doses.

Sustaining the mood-enhancing effect of ketamine and interactions with other substances

The studied Bluelight community is trying to find ways to sustain the mood-enhancing effect of ketamine. The transient aspect of this effect is considered a big problem. Because of that, members report using ergoloid mesylates (T6), magnesium, zinc (T1) and gabapentin (T6) to extend the duration of this effect, with debatable results (see Q33).

There is some controversy on this topic. For example, using ergoloid mesylates (trade name "hydergine") to extend the mood-enhancing effect of ketamine was successful for some members (see Q34), but it caused negative effects for others (see Q35).

Discussion

Despite having several negative effects, the examined discourses considered the use of ketamine to elevate mood both efficient and worthwhile among individuals dealing with self-reported depressive symptoms. The positive results obtained with ketamine for coping with depressive symptoms, as described by the analyzed reports on Bluelight, are corroborated by a vast scientific literature (4,9,10,13,16,17,21,25–31,57,58).

The ability to promote both structural and functional plasticity in the brain has been hypothesized to underlie the fast-acting antidepressant property of ketamine. Indeed, the atrophy of neurons caused by chronic stress plays a key role in the pathophysiology of depression. Ketamine can change the neuronal structure, resulting in less depressive symptoms. Hence the term "psychoplastogen" to refer to drugs that display plasticity-promoting properties, such as ketamine and serotonergic psychedelics (8,59). In the analyzed discourses, the terms "re-wire" and "reset" were used to describe this neuroplasticity-promoting property of ketamine.

When it comes to suicidal ideation, the analyzed reports appraise the instantaneous antidepressant effect of ketamine as a convenient tool to alleviate it. This is in line with the scientific literature. For instance, in a study conducted by DiazGranados et al. (2010), 40 minutes of a 0.5 mg/kg ketamine IV infusion improved the clinical situation and it remained improved for up to four hours post-infusion (17). Moreover, with a smaller dose (0.2 mg/kg intravenously over one to two minutes), Larkin and Beautrais (2011) also describe the feasibility and efficacy of ketamine as a rapid-onset antidepressant in the emergency department (60).

It has been described that depression and PTSD share a common neural circuitry and have high comorbidity (61–63), which explains the fact that several Bluelight members reported having more than one mental disorder, with ketamine alleviating the overall symptoms caused by them. Ketamine works so well in a clinical setting that drug developers have been working to make next-generation alternatives, armed with a preliminary hypothesis for how the drug lifts mood (64).

The different routes of administration of ketamine were a topic of remarkable interest in the selected threads. The studied Bluelight members reported having positive results using mainly the intranasal route.

The recreational use of ketamine should not be confounded with the clinical use of it. First, using a drug in a medical setting prevents self-medication and allows extensive monitoring of the patients' responses to it. Second, the doses used to treat depression (usually 0.5 mg/kg IV, so 35 mg for a person with 70 kg) are much lower than the doses used by heavy users (which can reach one gram of ketamine per day). It is very important to make this distinction because one of the main concerns surrounding the approval of ketamine as an antidepressant is due to its ability to develop

dependence. Therefore, monitoring patients is an essential part of the treatment, especially when the patient takes the intranasal spray or oral tablet home; these two formulations present the risk of leading the patient to self-administer higher doses than prescribed and/or to use a different route of administration in order to potentiate the effect, as found in the analyzed reports. Bluelight members showed concern with the potential of ketamine to cause tolerance, addiction and adverse effects, hence several posts were dedicated to warnings about risks and harm reduction techniques.

A solution to this problem might be the administration of ketamine in a clinic, because it presents a protective factor in avoiding the development of addiction, managing side effectsand providing proper monitoring of the patient.

Furthermore, frequent use of high doses of ketamine can lead to the so-called K-bladder (damage to the bladder tissue, causing the K-cramps) and other urinary tract problems. In a very severe scenario, it can result in bladder removal (65,66). This is also confirmed by the examined posts on Bluelight, where the urinary tract was mentioned as the most damaged by ketamine misuse.

Scientific data show that, in a clinical setting, the applied doses of ketamine are well-tolerated by humans and its negative effects are manageable. These effects seem to be dose and frequency-related, which is strongly supported by the scientific literature (9,20,21,28,31,67,68) and by the analyzed threads, where the adverse effects of ketamine were mentioned as mild and manageable. Addiction is considered an exception and harm reduction orientations are an important part of the analyzed discourses, as previously discussed.

Strategies to sustain the mood-enhancing effect of ketamine are not only being discussed in the academic field, but they are also subject of concern of the members. Few studies have systematically followed patients beyond 72 hours post-ketamine. It is unclear why many patients showing a response at 24 hours post-ketamine relapse less than 48 hours later while some patients maintain their response for several weeks. A tactic applied by some Bluelight members to preserve ketamine's effect is to keep using it occasionally. This agrees with results from institutional research and ketamine clinics are already applying this protocol. An open-label trial from 2010 administered six ketamine IV infusions in the course of twelve days; the authors concluded that multiple ketamine infusions can provide prolonged benefit (69). Furthermore, another open-label trial applied six ketamine IV infusions in the course of six months in 28 patients with TRD; it has concluded that repeated low dose ketamine infusions can be safely given, with positive results (26).

The investigated discourses raised the hypothesis that a combination of ketamine and magnesium can prolong the mood-enhancing effect of ketamine. Indeed, both affect NMDA signaling and this combination might be clinically useful, and possibly more effective than either compound alone, which was already tested and confirmed (70). Nevertheless, the scientific literature does not describe this same effect with zinc (71,72). Riluzole was previously used in an attempt to maintain the effects of ketamine, but it failed to provide any benefit over placebo (73). Regarding gabapentin, Yasmin et al. (2001) have found that it may be of adjunctive benefit in the management of TRD (74). No further conclusions about it can be drawn from the analyzed threads, because the use of gabapentin for this purpose was controversial. Finally, ergoloids are used by many people as a nootropic, commonly in conjunction with other cerebral enhancers, like piracetam (75). An article from 1989 (76) describes better antidepressant response in MDD patients pretreated with ergoloid mesylates before ECT. In the present study, only one T6 member described good maintenance of ketamine effects with ergoloid mesylates.

Regarding the limitations of this study, one is the fact that we do not know whether the authors of the analyzed posts are actually clinically depressed. Moreover, we analyzed only one online forum, whereas there are several others. Furthermore, despite the inevitable issues of authenticity, validity and reliability that are associated with online research of user-generated content, on online drug forum communities there are some well-informed users who appear to provide reliable information about compounds and combinations. Some experienced members display a high level of knowledge, as also seen in several other studies (42,43,45,77–80), with particular highlight to the technical and pharmacological properties of novel compounds and in identifying unknown active ingredients of new products (43,77,79). The information posted in the analyzed online forum shows synchrony with scientific data, leading to the conclusion that the stereotypical image of the "drug misuser" may need to change (80). Considering that ketamine has a potential for misuse and addiction, it would be important, in the future, to examine also threads on general use of ketamine. In our study we have only focused in the reported use to cope with depression and PTSD.

Qualitative sampling does not privilege the numerical aspect, but the ability of the sample in reflecting the phenomenon in its multiple dimensions (81). The social actors who possess the knowledge that the researchers want to explore constitute the sample in qualitative research. Thus, qualitative studies use intentional samples, which means that cases with rich

information about the studied theme are selected (52). In the current study, we found some of these actors on Bluelight. Considering it used an intentional sample, the results of this study cannot be generalized, neither used to represent the whole population of ketamine users. However, it does reflect the perspective of users as a comparison to the perspective of the prescribers.

Ketamine appears to be a potential tool in managing depressive symptoms. The increasing popularity of the ketamine clinics and the FDA approval of esketamine for TRD say a lot about the current status of off-label ketamine: it seems to work in several situations and people are already benefiting from it (not only people living with depression or PTSD; another popular off-label use of ketamine is for treating chronic pain). Ketamine has the potential to benefit a big group of patients who do not respond to the available therapies. It is considered by the World Health Organization an essential medicine and restricting it has harmed patients, with no reduction in recreational use. More scientific research is needed, naturally, but there is already a substantial amount of data suggesting that ketamine is effective and safe. *"If they don't bring us the treatment, we will make it ourselves"*, a T1 member stated. From the black market to the white coat, ketamine as a mood enhancer has been presenting positive results in handling depression and PTSD, giving a novel approach to the pathophysiology and therapy of these conditions.

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