

'Impressed With Impact' of Ketamine in Cancer Palliative Care

Kate Johnson

January 27, 2020

Like many in her field, Toronto psychiatrist Madeline Li, MD, PhD, was skeptical when one of her psychiatry residents suggested they launch a study into the effects of ketamine for depression in cancer palliative care.

But now, after treating about 15 patients, she's a convert.

"When I saw what it did, it was remarkable," said the clinician-scientist in the Department of Supportive Care at the Princess Margaret Cancer Center in Toronto, Canada.

Today, she is running the only [registered study](#) to investigate ketamine specifically for the treatment of depression in cancer patients.

Although the team has recruited only five patients so far, "they have all had remarkable results," she reported. "Within 1 hour of the first dose, they feel different, and they're not even sure how to describe that. I have been so surprised."

The study aims to enroll 20 patients to assess feasibility for a randomized, placebo-controlled trial.

In the meantime, on the basis of her observations, Li has started offering ketamine to her other cancer patients with moderate to severe depression. "I've now tried it on maybe 10 outpatients off label, and it's worked for maybe six of them, so not all of them."

One of the patients for whom it worked was Jim Newman, 78. His reaction to ketamine was a game changer, says his wife, Louise Roberge.

Jim had esophageal cancer, and an emergency esophagectomy in October 2018 left him unable to eat, drink, or even swallow, she told *Medscape Medical News*.

"He came out of the hospital with an estimated 8 to 13 months to live, and he's now lived 14 months," she said, smiling. "He's beaten the odds."

However, during those months, her husband sank into a fatigue-fueled depression, she said. Two rounds of chemotherapy left him so sick that he abandoned the treatment, and his previously active lifestyle was snatched away. Skiing, golfing, tennis, fishing — all were out of reach. "When Dr Li offered ketamine, we thought, what is there to lose?" she said.

She never imagined how much they would gain.

"I got my husband back," she said, flipping through the photos of this past summer on their boat, his day out on the golf course, and the fish he caught with his buddy.

"Even after the first half dose at the hospital...what a big difference," she said, laughing. She described how Jim's veil of depression lifted and how he looked up and spoke to her.

Jim agrees that the drug was transformative. "The reaction I had almost instantly — and it was almost instantly — was that I didn't seem to be depressed," he told *Medscape Medical News*.

"I don't really remember what I was like before, but I know I started off very negative," he said. In fact, he had sought and gained approval to receive Medical Aid in Dying (MAID), an option which he subsequently postponed after starting the ketamine regimen.

Off-Label Use of Ketamine

Ketamine is an old drug. It was initially approved by the US Food and Drug Administration (FDA) in 1970 as an anesthetic agent that was administered intravenously or intramuscularly for use in diagnostic and surgical procedures. It is now available generically.

It is used off label in the treatment of [resistant depression](#) and intractable pain and was recently assessed for the treatment of [problem drinking](#), as reported by *Medscape Medical News*.

In addition, it is a drug of abuse that is popular on the club scene. It is often referred to on the street as Special K.

A new product, esketamine (*Spravato*, Janssen), which is an enantiomer of ketamine that is administered intranasally, was [approved](#) by the FDA last year for treatment-resistant depression, although that approval raised some [concerns](#) among

experts.

Speaking to *Medscape Medical News*, Li suggested that ketamine may have a unique potential particularly for cancer-related depression.

"Often in palliative care, people's life expectancy isn't long enough for a standard antidepressant to take effect. You need something rapidly acting," she explained.

Another clinician in this field agrees. Also in Toronto, and less than an hour away from Li's clinic, another team is using ketamine to treat persons who have psychiatric disorders. Since June 2018 at the [Canadian Rapid Treatment Center of Excellence](#), ketamine infusion therapy has been offered to patients with major depressive disorder, bipolar disorder, posttraumatic stress disorder, or obsessive compulsive disorder.

The center is headed by Roger McIntyre, MD, who is also professor of psychiatry and pharmacology at the University of Toronto and is head of the Mood Disorders Psychopharmacology Unit at the University Health Network, Toronto.

He told *Medscape Medical News* that he is convinced of the benefits of ketamine in this patient population — which could easily include palliative cancer patients.

"It's a very interesting and appropriate area," he said in an interview. "People who are palliative need treatments that are not just effective but treatments that are extremely fast. Time is not on their side, and ketamine can work in 1 to 2 days. The other thing is that in the palliative care setting, a lot of these people also have pain, and ketamine has been used for decades to treat pain. So there's a couple of reasons right there why it is entirely appropriate."

Unique Delivery

Although others have delivered ketamine intravenously, Li has devised a unique way of delivering it via a nasal atomiser.

"The FDA has approved a nasal dose of esketamine, but if you look at the studies, esketamine is not as good as ketamine," she said. "As part of my study, we use an atomizer, and we draw up the solution that is used intravenously and we spray it [inside the nose]."

Patients on the hospital palliative cancer ward are eligible for the study if they have moderate to severe depression. They are treated on days 1, 5, and 7 with a starting dose of 50 mg administered intranasally. The dose is escalated to 50–100 mg and then to 100–150 mg.

On day 8, the primary outcome is assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS). Treatment is then stopped.

"Another primary objective is to see how long the effect lasts, so we measure the MADRS again on day 10 and 14, and we generally see depression returning by day 14, at which point patients have the option of continuing if they want," said Li.

Most patients end up with a twice-weekly dose, with sustained effects.

"That's the piece that I find so convincing," said Li. "It's not like giving them cocaine and they feel better for a few hours. There's actually a sustained benefit over several days."

The results are not just quantitative, she added.

"It's qualitatively where I am just so impressed with the impact of this medication. Family members will say, 'I haven't seen him or her look like this in months. They're so much more relaxed, they're smiling all the time, they have so much more energy.' It's the family members who notice it and tell me, 'This is miraculous. It's a marked improvement.'"

It's qualitatively where I am just so impressed with the impact of this medication. Dr Madeline Li

In the current "psychedelic renaissance," ketamine has so far stayed off the radar for palliative care depression, partly because it is normally administered via intravenous infusion over a number of hours — which tends to be too invasive for this frail patient population — but mostly because it has largely been overshadowed by the more classic psychedelic psilocybin.

A few small studies that have examined psilocybin for the treatment of depression in cancer patients have shown impressive results, with some suggesting it is a [game changer](#).

There is likely a role for both of these drugs in the treatment of cancer-related depression, because the drugs are very different chemically and produce very different results.

"The classic psychedelics, including psilocybin, work at the serotonin receptor, while ketamine works at the NMDA [*N*-methyl-D-aspartate] receptor," explained Daniel Rosenbaum, MD, a University of Toronto psychiatry resident. He is the lead author of a recent review of the topic entitled "Psychedelics for Psychological and Existential Distress in Palliative and Cancer Care" (*Curr Oncol* . 2019;26:225–226).

The benefits of classic psychedelics such as psilocybin are that they trigger "mystical-type experiences," he explained.

"Mystical-type experiences are characterized by core features of unity, a noetic quality (that is, the sense of encountering 'ultimate reality'), sacredness, deeply-felt positive mood, transcendence of space and time, and ineffability (that is, the sense that the experience cannot be adequately described using words)," he writes in his review.

In contrast, ketamine given in antidepressant doses "results in 'mostly ordinary consciousness,' " he continues.

"People will say they feel a little floaty, but it's not an out-of-body dissociative experience or anything like what's described with psilocybin," said Li. "They are not high, they have not had some deeper connection with the earth or the afterlife – and the next morning they are as surprised as their family about how much better they're feeling."

And while a psilocybin "trip" takes many hours and is combined with drug-assisted psychotherapy, the ketamine treatment involves just a squirt up each nostril.

"I think the target is different," Li said of the two drugs. "Ketamine is actually an antidepressant, but psilocybin is targeting existential distress — there is something about a transcendent experience that can make you less afraid of dying."

What she has found interesting, however, is that ketamine has also helped some of her patients with facing death. Whereas some, like Jim, have postponed their option for MAID after taking ketamine, others have embraced it.

"For some people, once their depression lifts, they actually think more clearly and feel less guilty about their decision to go ahead with it," she said. "I had one patient who was approved for MAID but was worried about setting a date because her family was against it, and she felt guilty about choosing to leave them earlier than she needed to. After we removed the depression with ketamine, she felt, 'This isn't the quality of life I want. I'm really, really sure of it now. My family is going to lose me anyway, and their grief won't be different whether I go through MAID or naturally, and so I am setting a date.' "

Li hopes her current feasibility study will lead to a randomized trial, although so far it has recruited only five patients, which is the same number as the only other study that investigated ketamine (a single oral dose) in cancer depression. That [study](#) was terminated early in 2014 after 2 years and slow accrual, but the results were less positive than what Li is seeing.

"I wish I had information that would be helpful," commented the lead investigator of that study, Robert Bright, MD, from the Mayo Clinic in Scottsdale, Arizona. "One patient became nauseous and vomited the administered dose soon after taking it. No one had any psychotic or dissociative reactions, and I did not see anyone with remarkable improvement. The blinding was never broken, so I don't know who got placebo vs ketamine."

For more from Medscape Oncology, follow us on Twitter: [@MedscapeOnc](#).

Medscape Medical News © 2020

Cite this: 'Impressed With Impact' of Ketamine in Cancer Palliative Care - *Medscape* - Jan 27, 2020.