Overview of Midazolam Use February 2, 2021

This brief addresses the use of midazolam in Canada in the context of Medical Assistance in Dying (MAID) and how it differs from its use in some States in the United States of America (USA) in the delivery of State mandated capital punishment.

In Canada, midazolam is a drug that has a wide variety of protocol guided applications in medicine. For example, it is used to provide anxiety relief and sedation during various procedures such as for a colonoscopy and is frequently used in dentistry to provide sedation and reduce anxiety. Midazolam is also used as part of anesthesia protocols in major surgery for the same purposes.

In addition, midazolam is commonly used in palliative care and MAID to provide anxiety relief and sedation. These uses are guided by protocols which can be requested from the health authorities in which these interventions are provided.

All the protocols that guide the use of midazolam in Canada are significantly and substantially different than the use of this drug in capital punishment application in the USA.

To help understand this difference it is essential to appreciate that drugs can have different effects at different doses. This includes therapeutic effects and toxic effects. It is the dose and how it is delivered that matters.

For example, the drug lidocaine, which is used to control pain and some types of heart irregularities, demonstrates different effects at different doses. At low doses, when injected into tissue such as skin or gums, lidocaine can dull the pain associated with minor surgical procedures, such as removal of some types of skin cancer or dental procedures such as tooth extractions. In cream or patch format, low doses of lidocaine are used to treat minor skin irritation (such as insect bites), to help relieve the pain of shingles and even to dull the needle prick pain in childhood vaccinations. At increased doses, lidocaine delivered intravenously (IV) is used to treat some heart irregularities. At higher doses, lidocaine can cause a host of negative effects including dizziness, blurred vision and seizures. At very high doses, delivered IV, it can lead to death. Clearly, the impact of this drug is dependent upon the dose used and the way the dose is delivered (cream, patch, injection or IV).

The same is true for midazolam.

In Canada, midazolam is used to provide relief from anxiety and to induce clinically required sedation. In Canada, it is used intravenously following scientifically established protocols at different doses in different situations to achieve these results. For example, at low doses (usual IV dose of 2 – 4 mg) it is used in procedural sedation such as for a colonoscopy or a dental extraction. At slightly higher doses (usual IV dose of 5 – 20 mg) it is used in the first phase of anesthesia induction, palliative care and MAID. Its use in all these various indications is to provide relaxation and sedation, NOT to bring about death. Very rarely, mild side effects such as a transient feeling of restlessness may occur at these doses.

4. Midazolam has an important property not mentioned in the brief of February 2, 2021 and that is to produce amnesia.
5. Amnesia is the principal reason Midazolam is utilized in the clinical setting.
6. The production of amnesia in the setting of MAID is moot.
7. The use of Midazolam to provide comfort in anticipation of voluntarily being put to death for the purposes of the relief of intolerable suffering seems to only delay the purpose of MAID.
8. In the United States, Midazolam is not used to produce death in the setting of lethal injection.
9. In the United States, Midazolam use in lethal injection has been associated with the findings of lung congestion as seen on autopsy.
10. The report of Midazolam not causing harm in the setting of MAID is a claim without evidence and is unverifiable.
11. MAID provider reports that death by MAID appears peaceful reflects a serious lack of understanding on the part of those providers about the mechanism of action of muscle relaxants like rocuronium.
12. Propofol may or may not produce death when injected as specified in MAID.
13. Propofol may or may not induce a state of lack of awareness when injected as specified in MAID.
14. Propofol has not been used for lethal injection in the US but in the clinical setting, patients complain of a burning sensation in the injection site when injected with a dose that is $1/10^{th}$ (100 mg) the dose used in MAID.
15. Propofol injection at a dose of 1000 mg as used in MAID very likely causes burning in the lungs and tissue destruction as can be observed with the injection of pentobarbital or Midazolam in the setting of lethal injection for execution.
16. Muscle relaxants, when injected in MAID, will produce an outwardly observed stillness as a consequence of muscle paralysis than has wrongly and repeatedly been described as a state of peacefulness.
17. Muscle relaxants when used in MAID will produce death by suffocation.
18. The MAID protocol very likely causes lung congestion in a similar fashion to that which has been shown in over 200 cases of lethal injection in the US.
19. The only way to refute the hypothesis that the MAID protocol causes pulmonary fluid accumulation and death akin drowning is by obtaining Canadian data through autopsy studies on at least 200 individuals put to death by MAID.
20. In the setting of lethal injection in the US, individuals involved in intravenous catheter placement and injections must have appropriate and relevant training to perform these tasks and are generally supervised by a physician.

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For greater clarity, midazolam use in both palliative care and MAID is to provide comfort to the patient - it is not used to bring about death. Its use in MAID protocols is similar to its use in procedural sedation, anesthesia and in palliative care protocols.

In a typical Canadian MAID protocol, midazolam at a dose of 10 – 20 mg IV is administered first to provide relaxation and sedation, followed by a small amount of lidocaine to ensure that the next medication to be used does not cause transient IV site pain or irritation to the vein when injected. The next medication is propofol at a dose of 1000 mg IV, which is about five to ten times the amount used for inducing general anesthesia. This drug places the person in a deep medically induced coma. Finally, another drug is administered to stop the activity of the breathing muscle, the diaphragm. The cessation of breathing causes the heart to stop.

This procedure and use of midazolam for MAID in Canada is completely different from that used in lethal injections in the USA. Although State execution protocols in the USA vary from State to State and may change within a State over time, midazolam is not usually used to carry out death, although it has been used in some States at some point as the agent for causing death. In cases where midazolam was used as the drug causing death, the dose used is at an extremely high amount: 500 mg given IV. At that extremely high amount the drug can potentially cause problematic breathing problems before breathing stops. This is the issue that has raised concerns about using these extremely high amounts of this drug for that purpose in the USA.

It is essential to understand that this is not how midazolam is used for any purpose (including in palliative care or MAID) in Canada and this toxic effect does not occur in MAID protocols that apply the doses of this drug as described above.

For greater clarity, the dose of midazolam used in Canada for relaxation and sedation during MAID is between 2% and 4% of the dose used for death causing purposes in the USA. At the doses typically used in Canada (10 – 20 mg IV), midazolam does not cause the toxic effect phenomenon observed when 500 mg IV is used.

A further point of clarification is related to who is administering midazolam. Within Canada only physicians or nurse practitioners are eligible to administer medications for the purpose of MAID. This ensures that highly qualified professionals with the knowledge, skill and judgment to monitor and determine the effectiveness of the medications are present and can make necessary adjustments. In the USA each capital punishment delivering State has a different protocol, and very few of these protocols require the presence of a physician or nurse practitioner. For example, in Texas where the majority of lethal injections take place in the USA, the protocol only requires one licensed professional to be present and that person could be from any of the following categories: certified medical assistant, phlebotomist, emergency medical technician, paramedic or medical corpsman. These providers are neither doctors nor nurse practitioners.

Within Canada midazolam is administered for MAID in doses that are designed to provide comfort to the person, not to cause death. It is administered by highly trained health professionals (doctors and nurse practitioners) who are able to understand the intended use and possible side effects and toxic effects of the drug. In Canada, using the established protocols, there have been no reports of midazolam causing a harmful effect during a MAID death.

Senator Kutcher, Senator Mégie, Senator Moodie, Senator Ravalia

Peer review conducted of the information used in this brief by numerous physicians (anesthesia; primary care; internal medicine; palliative care; MAID provision, emergency medicine, pediatrics), nurse practitioners and pharmacists from Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Ontario, Quebec and British Columbia.

ATTN: Mark Palmer
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In reply to: Overview of Midazolam Use
February 2, 2021
Senator Kutcher, Senator Megie, Senator Moodie, Senator Ravalia

February 8, 2021

Preamble: My name is Joel B. Zivot and I am a licensed physician in the state of Georgia, USA. I earned my medical degree from the University of Manitoba in 1988. I have held unrestricted medical licenses to practice medicine in the provinces of Manitoba and Ontario. I am a fellow of the Royal College of Physicians of Canada with the specialty of Anesthesiology. I am board certified in Anesthesiology and Critical Care Medicine by the American Board of Anesthesiology. I have been a practicing anesthesiologist and intensive care medicine specialist for the last 26 years. I am an expert in the use of the drugs mentioned in this brief. I estimate I have provided anesthetics and sedation to over 50,000 people.

The above-mentioned brief, dated February 2, makes the following claims.

1. With respect to the spectrum of action of Midazolam, some variation occurs depending on dosage adjustments.
2. For the purpose of MAID, Midazolam is intended to provide “relief from anxiety” and to provide “comfort to the patient”.
3. Midazolam is not used in MAID to produce death.
4. When Midazolam is used in lethal injection for execution in the US, the purpose of Midazolam is generally to produce death.
5. In the setting of MAID, Midazolam is administered by highly trained health professionals and this is different from the qualifications of those that administer Midazolam in the setting of lethal injection for execution.
6. There have been no reports of Midazolam causing a harmful effect during a MAID death.

The February 2 brief misses the point, fails to address critical questions or is wrong for the following reasons:

1. Lethal injection for execution and MAID are fundamentally identical tasks in that both are designed to cause death by the use of the injection of medications not specifically designed to be used to produce death.
2. No Pharmaceutical company develops or markets medications to be used to produce death in people.
3. The package inserts for Midazolam, Propofol and Rocuronium do not list MAID as an indicated uses and make no mention of dosage for the purposes of MAID.

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20. In the setting of lethal injection in the US, individuals involved in intravenous catheter placement and injections must have appropriate and relevant training to perform these tasks and are generally supervised by a physician.

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