Geisinger Medical Center

Methadone switching for refractory cancer-related pain

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Abstract

Background:

Methadone is an effective medication for treating pain and has unique characteristics that require specialized knowledge to prescribe safely.
Patient history:

A 57-year-old male with metastatic castration-resistant prostate cancer was experiencing pain not controlled with a total buprenorphine dose of 32 mg per day. Six months later, the cancer progressed, and his pain stopped responding to buprenorphine. He was started on methadone 10 mg (10% of the MEDD) every 3 hours as needed per the Morley-Makin dosing protocol. He required, on average, 30 mg of methadone a day.

A second patient with rectal cancer was transitioned from 32 mg buprenorphine to 120 mg methadone/24 hrs. A third patient with oral cavity SCC on buprenorphine (required total 12 mg buprenorphine/24h) was transitioned from buprenorphine to methadone 20 mg once to twice daily with adequate pain control.

Conclusion: The conversion from buprenorphine to methadone for cancer pain has not been reported. We found that using an as-needed dosing strategy allowed for a safe transition with a conversion ratio of 1mg of buprenorphine to 4-2mg of methadone.

Introduction

Buprenorphine has a unique receptor binding profile with a higher binding affinity to the mu opioid receptor when compared to traditional opioids. It is a partial agonist with high affinity at the mu opioid receptor, reverse agonist at the delta kappa, antagonist at the delta and with lower affinity the ORL1 that may contribute to analgesia but at the same time less adverse effects such as respiratory depression, sedation or cognitive impairment

One of the unique properties of buprenorphine is its chaperone effect which results in an increase in MOR expression on cell surfaces. This may potentiate the responses to opioids which are subsequently used in rotation . Though most patients respond to buprenorphine a subset of patients with the N40D MOR mutation poorly respond to buprenorphine
There is little known about the conversion ratio from sublingual buprenorphine to potent opioids. The morphine to SL buprenorphine ratio is approximately 50 to 1 and the oral oxycodone to SL buprenorphine ratio is 34 to 1 in the few studies that have reported such conversions. It would be anticipated therefore at standard doses (< 100mg/d MEDD) that the ratio of SL buprenorphine to methadone would be approximately 1 to 10
We recently had 3 patients poorly responding to SL buprenorphine whom we converted to methadone using a Morley-Makin as needed dosing strategy using 10mg every 3 hours as needed

Dose Ratios

Dose ratio of the previous substitution drug to slow-release oral morphine (1:x).

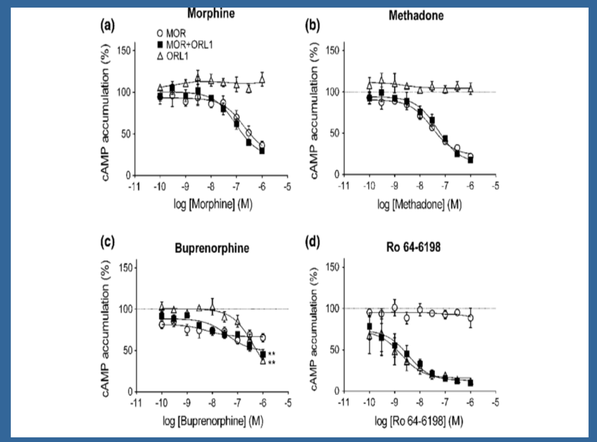
Day	Racemic Methadone	Levomethadone	Buprenorphine
1	8.3	13.8	42.3
2	9.1	15.0	51.5
3	9.7	15.7	52.1
4	10.5	16.0	56.4
5	10.5	16.4	56.2
6	11.2	16.5	54.7
7	11.4	16.9	58.3
8	11.6	17.0	56.8
9	11.7	17.1	55.7
10	11.6	17.2	56.0
11	11.7	17.2	56.9
12	11.7	17.3	55.7
13	11.7	17.3	57.1
14	11.8	17.4	58.0

Patients Histories

A 57-year-old male with metastatic castration-resistant prostate cancer was experiencing pain not controlled with the use of tramadol and acetaminophen. His initial analgesic regimen by Palliative Medicine was morphine sulfate extended-release 30 mg twice a day. Despite further titration of morphine sulfate and treatment with radium 223, the pain remained sub-optimally controlled. Buprenorphine micro-dosing was initiated, and morphine was discontinued. Adequate analgesia is achieved with a total buprenorphine dose of 32 mg per day. Six months later, the cancer progressed, and his pain stopped responding to buprenorphine. He was started on methadone 10 mg (10% of the MEDD) every 3 hours as needed per the Morley-Makin dosing protocol. He required, on average, 30 mg of methadone a day. The patient was discharged home with hospice care and died after a month at home. Pain remains adequately controlled with methadone.

A second patient with rectal cancer was transitioned to buprenorphine and had adequate analgesia achieved with 32 mg buprenorphine, but his pain resurged due to cancer progression. Using the methadone 10% MEDD q3h as needed strategy, the pain came under adequate control on 120 mg methadone/24 hrs.
A third patient with oral cavity SCC on buprenorphine (required total 12 mg buprenorphine/24h) was transitioned from buprenorphine to methadone 20 mg once to twice daily with adequate pain control.

MOR Availability and Dose.



Discussion

Our first patient was on SL buprenorphine 32mg/day and became comfortable with 30mg of methadone a day (a conversion ratio of 1 to 1). Our second patient was on SL buprenorphine 32 mg/day and was converted to 120mg of methadone/day (a conversion ratio of 1 to 4).. Our third patient was on SL buprenorphine 12mg/ and was converted to methadone 20mg/ d (a conversion ratio of 1 to 1,6).

We believe that in patients with a severe cancer patient on high-dose buprenorphine, a safe conversion can be accomplished through an as-needed dosing strategy using methadone at 10mg every 3 hours as needed. Dosing should remain as needed for at least 6 days due to the half-life of methadone. This can be accomplished at home with a reliable caregiver and frequent calls or visits. The conversion ratio is likely to be lower than anticipated, which is either due to the chaperone effect of buprenorphine or individuals who do not respond likely have the N40D mutation, which does not impair methadone analgesia

Conclusions

Patients on high-dose SL buprenorphine can respond well to methadone at lower-than-anticipated conversion ratios. An “as needed” dosing strategy would be optimal for this case.
Analgesic responses may occur at lower than anticipated doses of methadone, presumably related to buprenorphine chaperone effects on MOR.

References

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