

Buprenorphine: Opioid Agonist-Antagonist Benefits for Opioid Resistant Pain, Uncontrolled By Full-Agonist Opioids During Hematopoietic Stem Cell Transplant for Sickle Cell Disease

BACKGROUND

- Bone marrow transplant (BMT) offers potential cure for cancer and a spectrum of otherwise incurable diseases. However, the **BMT** complications lead to multi-systemic PAIN presentation.
- Sickle cell disease (SCD) is a hematologic disease with life-long pain from infancy. Because of frequent pain resulting in hyperalgesia and chronic opioid use, SCD patients undergoing BMT often experience excruciating pain uncontrolled by rapid escalation of opioid dosing and numerous adverse effects.

Pain Related to BMT:

- Neuropathic Pain / Paresthesia / Headache
- Myalgia / Arthralgia / Bone Pain / Visceral Pain
- Mucositis Pain / Dyspepsia / Dysphagia / GVHD
- Inflammatory-Infection Pain / Radiation Injury Pain

Repetitive Exposure to Pain and Opioids Results In:

Opioid dose escalation \rightarrow More side effects \rightarrow CHRONIC pain \rightarrow Central sensitization \rightarrow fear, anxiety \rightarrow ED / hospitalization

- Buprenorphine, an opioid with novel pharmacology > Partial Mu opioid Receptor AGONISM – High Affinity -> Less respiratory depression, Less euphoria, Slows tolerance, Less constipation, Leaves room for other opioids
- ➢ Kappa opioid receptor ANTAGONISM → Anxiolytic, addictive potential, immunosuppression, constipation
- \rightarrow Delta opioid receptor ANTAGONISM \rightarrow GI and respiratory SE
- ➢ Opioid Receptor Like 1 (ORL1) AGONISM → Preferred SPINAL Receptor action >> CNS R \rightarrow | rewarding effect, | tolerance
- **SAFE** in renal insufficiency and hepatic impairment.
- Significantly decreases acute care utilization.

OBJECTIVES

Growing body of literature have shown superior effect of **buprenorphine, Opioid Agonist-Antagonist**, over full-agonist opioids for chronic SCD pain in the outpatient setting.

A pilot prospective clinical trial for buprenorphine-based inpatient **pain management** was conducted for SCD patients' acute severe pain to assess for the inpatient use efficacy of buprenorphine in the setting of BMT, a significant pain escalation factor.

This trial was initiated after observing serial cases of SCD patients' BMT-related pain, uncontrollable by enormous doses of traditional opioids, remarkably resembling some patients with hematologic malignancy undergoing BMT.

MEDD: 24hr Opioid Requirement

Full-Agonist Opioid Analgesic Regimen

Buprenorphine **Based Opioid** Regimen

Table 2. Patient Demographics and Disease

Case	Age	Gender	Ethnic Background	Genotype
1	18	М	Nigerian	HgbSS
2	22	М	Nigerian	HgbSS
3	39	F	Congolese	HgbSS
4	19	М	African American	HgbSS
5	7	М	African American	HgbSS

Mayuko Sakae, MD | Clarke Anderson, MD

METHODS

• Buprenorphine was started as scheduled and as-needed analgesics IV, supplemented by full-agonist opioids for SCD patients enrolled in clinical trials with BMT upon consultation for uncontrolled pain.

• Patients' 24-hour opioid requirement by morphine equivalent daily doses (MEDD) were assessed at **3 time points**. (Table 1)

1) Before pain escalation; 2) Consultation day for pain; 3) Discharge day • MEDDs were retrospectively compared to those of SCD patients treated with full-agonist opioids only during their BMT admission.

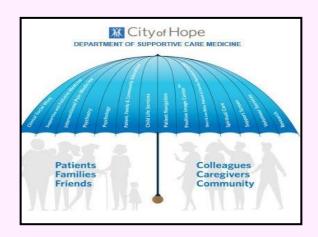
RESULTS

 Table 1. Morphine Equivalent Daily Dose (MEDD) for BMT Pain Management in SCD
 Patients Receiving Full-Agonist Opioids vs. Buprenorphine-Based Management

	Case	Pre-Consultation <u>MEDD</u> : Immediately Prior to Pain Escalation	Consultation Day <u>MEDD</u> : Pain Uncontrolled	Discharge Day Post-BMT MEDD: Pain Controlled (% Increase in MEDD)
	1	240 mg	840 mg	3192 mg (1230%)
	2	74 mg	170 mg	1220 mg (1548%)
	3	10 mg	352 mg	1640 mg (16300%)
е	4	30 mg	40 mg	125 mg (317%)
	5	7.5 mg	22.5 mg	24 mg (220 %)

- BMT-related pain.
- SCD patients.
- specifically cancer patients.

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RESULTS

Cases treated only by full-agonist opioids (morphine / fentanyl hydromorphone / methadone / hydrocodone / oxycodone) had escalation of MEDD by 1230 - 16300% by discharge date compared to the time point immediately prior to escalation of

Buprenorphine-supported cases had remarkably smaller MEDD increase by 220 - 317%. (Table 1)

CONCLUSIONS

 Our data suggests the benefits of potent pain control and limiting opioid tolerance by using Buprenorphine prior to fullagonist opioid dose escalation during BMT admission for

Buprenorphine may provide the advantages for treating pain of non-SCD patients with complex pain background and experiencing difficult pain management during BMT due to pre-existing hyperalgesia and high opioid-tolerance,

• We plan to develop a clinical trial of Buprenorphine-based complex pain management for cancer patients to compare with SCD cohort undergoing BMT.

REFERENCES