



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

KETAMINE-ASSISTED BUPRENORPHINE INITIATION

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UW PSYCHIATRY AND ADDICTIONS CASE CONFERENCE (UW PACC)

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DISCLOSURES

- Lucinda Grande, MD has an educational consulting contract with Peninsula Compounding Pharmacy
- Tom Hutch, MD has no disclosures

KETAMINE



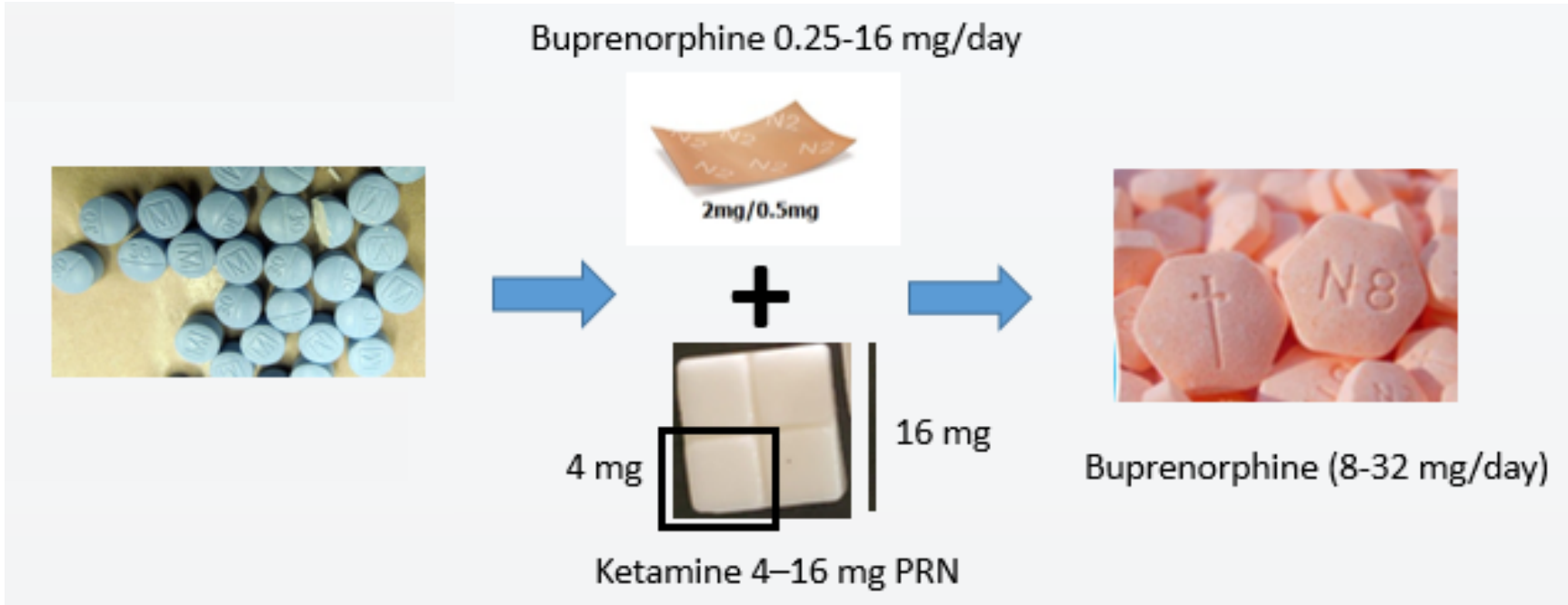
KETAMINE BRIEF INTRODUCTION

- NMDA receptor antagonist, FDA approved 1970
- Approved: dissociative anesthetic
 - Minimal respiratory depression at anesthetic doses
- Off-label:
 - Sedation for brief procedures, intubation, ICU ventilation
 - Agitation
 - Status epilepticus
 - Acute and chronic pain
 - Treatment-resistant depression

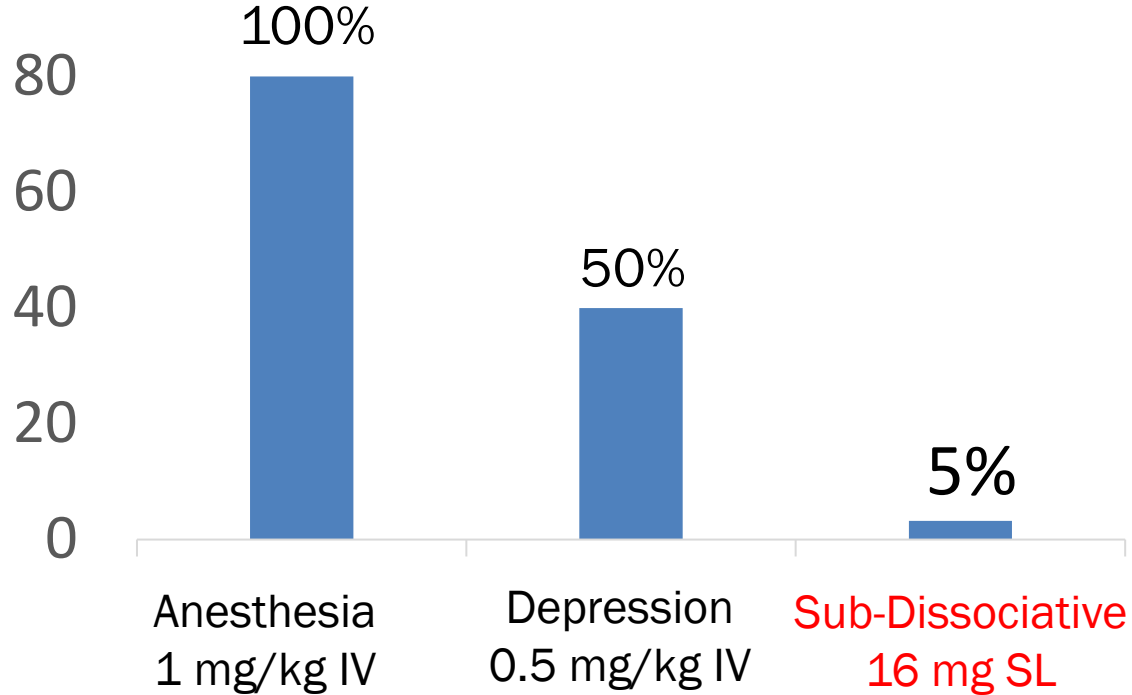
CINDY'S EXPERIENCE

- Ketamine (sub-dissociative dose, oral and sublingual)
 - 12 years, 600+ patients: chronic pain and depression
 - RCT of ketamine for chronic pain in 32 subjects
 - 3 peer-reviewed publications (ketamine)
- Buprenorphine
 - 12 years, 1000+ patients
 - Co-founder and first Medical Director of the Olympia Bupe Clinic (2019-2021)
 - 3 peer-reviewed publications (buprenorphine)

KETAMINE-ASSISTED BUPRENORPHINE INITIATION (KABI)



KETAMINE DOSE



25% Bioavailable, 80 kg person

MECHANISMS OF ACTION



- Blocking the NMDAr rapidly reverses central nervous system adaptations mediating opioid dependence and tolerance
- Ketamine rapidly increases both the concentration and efficacy of endogenous opioids, thereby potentially functioning as a proxy opioid agonist

RESEARCH

Open Access

Ketamine-assisted buprenorphine initiation: a pilot case series



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KABI PROJECT - LOGISTICS

- We Care Daily Clinics: intake, prescribed bupe & comfort meds
- WCDC referred patients to Cindy for KABI
- Cindy prescribed ketamine and clonazepam
- Daily monitoring by Cindy & WCDC team, telemed & in-person
- Ketamine dispensed by local compounding pharmacies
—\$20-25 for each patient
- Support and follow-up care with WCDC team or Cindy

KEY DISCOVERIES

- 3 ways ketamine is useful during buprenorphine initiation:
 - To treat fentanyl withdrawal
 - To prevent BPOW (as premedication before bupe)
 - As treatment if BPOW occurs
- 16 mg SL works! (most of the time)
- Anxiety is not addressed by ketamine. Benzo is needed.
- Daily patient contact is essential

LEARNING PROCESS

- Lesson 1: Prophylactic pre-medication
- Lesson 2: Short induction duration
- Lesson 3: **Discontinue fentanyl, use ketamine for fentanyl withdrawal**
- Lesson 4: Use a benzodiazepine to prevent panic attacks
 - Clonazepam 1 mg daily x 4



OUTCOMES 5/2022 -7/2023

- 37 Patients: (22 F, 15 M), Ages 19-62, 2 methadone
- 24 patients tried ketamine and reported back
- 16 patients completed initiation
 - 43% of the 37 patients prescribed ketamine
 - 67% of the 24 who actually tried ketamine
 - 75% of the last 16 patients
 - 30-day retention among the last 16 patients: 92%

Earlier
12

Later
25

ID	Age	Sex	Referral source	Rx date	K doses	Troche or syrup	B/BN	Initiation style	Other meds	Fentanyl	Benzo	MTD	Days	BPOW severity	Completed	Bupe dose	30 day retention
1	26	F	OBOT	5/24/2022	10	troche	BN	micro fentanyl	Cl,G	-	-	-	5	none	yes	8	no
2	38	M	OTP	6/7/2022	4	troche	B	micro methadone	Cl,G	X	-	-	8	mild	yes	20	no
3	37	F	OTP	6/8/2022	4	troche	BN	micro fentanyl	Cl,G	X	-	-	-	moderate	no	-	no
4	25	F	OBOT	6/12/2022	16	troche	BN	high dose	chlordiaz	-	chlordiaz	-	3	mild	yes	16-24	no
5	19	F	OTP	12/5/2022	26	troche	BN	micro methadone	Cl,G	X	-	-	-	anxiety	no	-	no
6	37	M	OTP	12/6/2022	4	troche	BN	-	-	-	-	-	-	-	not disp	-	n/a
7	28	F	OTP	12/16/2022	4	troche	BN	-	-	-	-	-	-	-	disp no info	-	n/a
8	42	F	OTP	12/22/2022	4	troche	BN	micro methadone	Cl,G	X	-	-	-	-	no	-	no
9	35	F	OTP	1/19/2023	12	troche	BN	micro methadone	Cl,G	X	-	-	12	moderate	yes	XR-BUP	yes
10	39	F	OTP	1/30/2023	4	troche	BN	-	-	-	-	-	8	none	disp no info	-	n/a
11	43	F	OTP	1/31/2023	16	troche	BN	micro fentanyl	THC, Cl, G	X	-	-	-	anxiety	no	-	no
12	44	F	OTP	2/10/2023	8	troche	BN	d/c fent, traditional	Cl,G,L,O	+/-	-	-	4	mild	yes	24	yes
13	45	F	OTP	3/3/2023	28	troche	B	micro fentanyl	Cl,G,H,O,D	X	clonaz	-	36	anxiety	yes	24	yes
14	38	M	OTP	3/7/2023	8	troche	BN	-	-	-	-	-	-	-	disp no info	-	-
15	52	M	OTP	3/11/2023	8	troche	BN	d/c fent, high dose	Cl,G	-	-	-	3	severe	yes	8	yes
16	34	F	OTP	3/30/2023	8	troche	BN	micro methadone	Cl,G	-	-	X	6	moderate	yes	6 to 8	yes
17	36	F	OTP	4/26/2023	24	troche	BN	micro fentanyl	Cl,G,O,Z	X	clonaz	-	-	anxiety	no	-	no
18	27	M	OTP	5/9/2023	8	troche	BN	d/c fent, traditional	Alcohol	-	-	-	5	moderate	yes	XR-BUP	yes
19	37	M	OTP	5/16/2023	4	troche	B	micro methadone	Cl,G	X	-	-	-	severe	no	-	no
20	62	M	OBOT	5/22/2023	12	syrup	BN	d/c fent, high dose	Cl,G,T	-	-	-	4	anxiety	yes	XR-BUP	yes
21	49	M	OTP	5/30/2023	8	troche	BN	d/c fent, high dose	Cl,G, alcohol	-	-	-	4	anxiety	yes	16	yes
22	52	M	OTP	6/7/2023	4	troche	BN	-	-	-	-	-	-	-	not disp	-	-
23	42	F	pt ref	6/10/2023	8	syrup	BN	d/c fent, micro	Cl,G,C,T,O,D	-	clonaz	-	6	severe	yes	XR-BUP	yes
24	30	F	outreach	6/10/2023	8	syrup	B	-	-	-	-	-	-	-	disp no info	-	-
25	43	F	outreach	6/10/2023	8	syrup	B	-	-	-	-	-	-	-	disp no info	-	-
26	40	M	outreach	6/10/2023	8	syrup	BN	-	-	-	-	-	-	-	disp no info	-	-
27	54	M	OTP	6/14/2023	8	troche	BN	-	-	-	-	-	-	-	not disp	-	-
28	29	M	OTP	6/29/2023	8	troche	B	taper methadone	Cl,G	-	clonaz	X	6	moderate	yes	8	yes
29	45	F	pt ref	7/11/2023	16	syrup	BN	d/c fent, traditional	-	-	clonaz	-	3	mild	yes	XR-BUP	yes
30	43	F	OTP	7/11/2023	8	troche	BN	-	-	-	-	-	-	-	disp no info	-	n/a
31	47	F	pt ref	7/18/2023	16	syrup	BN	d/c fent, traditional	G,O,C	tiny bit	clonaz	-	3	anxiety	d/c fent	0	no
32	42	M	outreach	7/20/2023	8	syrup	BN	d/c fent,traditional	Cl,G,O,C	-	clonaz	-	5	severe	d/c fent	0	yes
33	55	F	OTP	7/25/2023	8	troche	BN	-	-	-	-	-	-	-	disp no info	-	-
34	40	M	outreach	7/25/2023	8	syrup	BN	-	-	-	-	-	-	-	not disp	-	-
35	27	M	OTP	7/28/2023	8	troche	BN	d/c fent,traditional	Cl,G	tiny bit	clonaz	-	4	mild	yes	24	yes
36	30	F	OTP	7/28/2023	8	troche	BN	d/c fent,traditional	Cl	-	clonaz	-	4	mild	yes	8	no



Procedure for a smooth 4 day initiation (Patients #30, #32, #36 and #37)

Day	Premedication	Ketamine + Buprenorphine	Optional
1 and 2	clonazepam 1 mg	Ketamine 16 mg as needed to treat fentanyl withdrawal (1-3 doses per day)	adjunctive medications
3	clonazepam 1 mg	(ketamine 8-16 mg then buprenorphine 2 mg) every 3 hours x 4	adjunctive medications
4	clonazepam 1 mg	buprenorphine 4 mg every 3 hours x 4	ketamine 8-16 mg premedication, adjunctive medications
5+		buprenorphine 8 mg, repeat as needed up to 32 mg	

Ketamine-Assisted Rapid Start LAI Bupe

- 4 patients so far, unique circumstances
- Ketamine and clonazepam premedication and 2-3 follow-up doses over the first 12 hours
- Ketamine also helps with the “icky” feeling of the next few days
- Could the antidepressant effects promote retention in treatment?

Engeriser Alabama Protocol

- 24-hour behavioral health crisis center
- 30 patients, 12+ hours since last fentanyl, COWS 9+
- Ketamine 10 mg IM
- Wait 30 minutes
- Buprenorphine 8 mg SL
- If w/d occurs, treat with buprenorphine, ketamine, clonidine

Engeriser Alabama Results

COWS (mean)

- Baseline 13.7
- 30 minutes after ketamine: 5.9
- 30 minutes after buprenorphine: 4.0

- Total buprenorphine administered first 4 hours: 9.6 mg
- 1 patient had severe withdrawal requiring overnight stay

KETAMINE-ASSISTED ONE-VISIT LAI BUPE START - NEW PROTOCOL



Lorazepam 1 mg PO +
Ketamine 10 mg IM



Buprenorphine 16 mg SL



Long-acting injectable
buprenorphine 300 mg SQ

Ketamine-Assisted One-Visit LAI Bupe Start - New Protocol (still being refined)

1. *Lorazepam 1 mg PO*
2. *LAI bupe 300 mg SC*
3. *Ketamine 10 mg IM*
Wait 30 minutes
4. *Buprenorphine 16 mg SL*

FUTURE PLANS

- Local clinics:
 - We can help you implement this treatment in your setting
cgrande@pioneerfamilypractice.com
tom.hutch@WeCareDailyClinics.com
- Formal research plans underway with Drs. Sackett & Saxon

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