LACK OF ANALGESIC EFFICACY OF OPIOIDS AND GABAPENTIN IN METHADONE AND BUPRENORPHINE MAINTAINED PATIENTS

Nielsen, S.[1,3], Murnion, B.[2], Demirkol, A.[1], **Rivas, C**.[1], Hayes, V.[1] & Lintzeris, N.[1,4]

1 Drug and Alcohol Services, South Eastern Sydney Local Health District
2 Drug Health Services, Sydney Local Health District
3 National Drug and Alcohol Centre, University of New South Wales
4 Discipline of Addiction Medicine, University of Sydney

BACKGROUND

- Pain management in opioid dependent patients is complex
  - Limited research informs guidelines
  - Current practice relies largely on expert opinion
- Aim: to identify the efficacy of three different analgesic strategies in patients receiving opioid agonist treatment
  - (1) additional methadone or buprenorphine
  - (2) oxycodone or
  - (3) gabapentin
- Model of experimental pain assessed by cold pressor tolerance

METHODS

METHODS

- Recruitment:
  - Patients on outpatient opioid agonist treatment clinic on stable dose for a minimum of 4 weeks
  - Two groups:
    - Methadone (dose 40 – 100mg)
    - Buprenorphine (dose 8 – 32mg)
- Exclusion criteria:
  - severe acute medical or psychiatric conditions, pregnancy, current use or dependence on other substances or participating in another research project, amongst others.

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METHODS

- Participants received, in random order and under double blinded conditions over 4 sessions, either:

1) Usual Methadone or Buprenophine (Control)
2) Usual MTD/BPN + 30% extra (MTD/BPN +30%)
3) Usual MTD/BPN + oxycodone (OXY)
4) Usual MTD/BPN + gabapentin (GPN)

- Oxycodone dose was intended to be equivalent to extra 30% methadone

Methadone dose	40mg	60mg	80mg	90mg	100mg
Oxycodone dose	10mg	10mg	15mg	20mg	20mg

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METHODS – session procedure

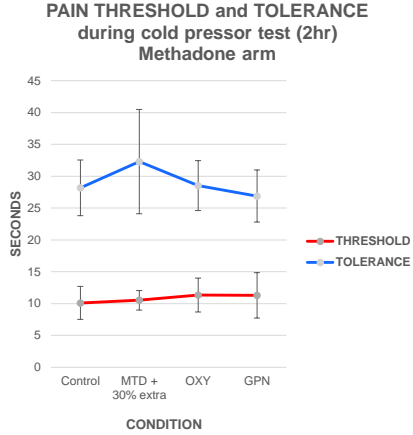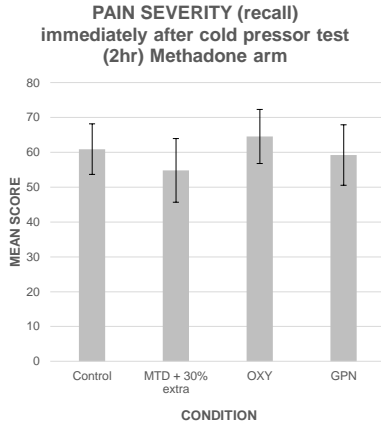| Baseline (t = 0) Opioid dose | t = 60min 600mg Gabapentin | T = 90 min Immediate release oxycodone | T = 2h Cold pressor test |

- Acute pain response measured by immersing the non-dominant arm in cold water at 5°C to above the elbow at time=2h (putative analgesic peak effect).

- Participants informed the research staff, when (a) pain was initially detected (threshold), and (b) they could no longer tolerate the pain (tolerance).

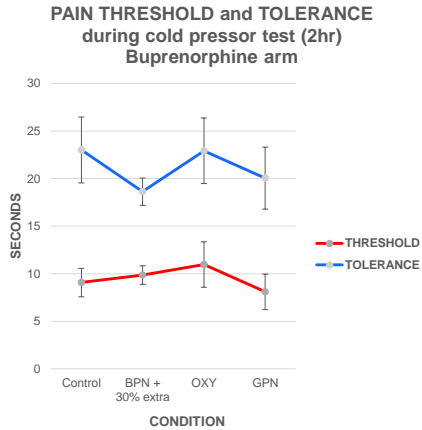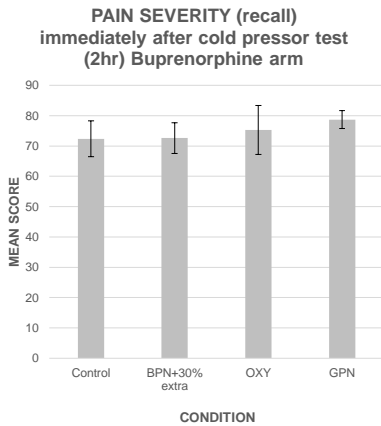- Data were analysed using linear mixed models, controlling for session order and opioid dose

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RESULTS

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Pain threshold/tolerance/severity (MTD)

PAIN SEVERITY (recall) immediately after cold pressor test (2hr) Methadone arm

PAIN THRESHOLD and TOLERANCE during cold pressor test (2hr) Methadone arm

*condition MTD + 30% extra significant at P<0.01 for Pain Severity

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Pain threshold/tolerance/severity (BPN)

PAIN SEVERITY (recall) immediately after cold pressor test (2hr) Buprenorphine arm

PAIN THRESHOLD and TOLERANCE during cold pressor test (2hr) Buprenorphine arm

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SUBJECTIVE MEASURES (VAS scales 0-100) pre cold pressor test (1hr50min)					
	Drug Strength Mean (SD)	Drug Liking Mean (SD)	Drug Sedation Mean (SD)	Drug Intoxication Mean (SD)	Drug Bad effects Mean (SD)
METHADONE GROUP					
Control (ref)	19.6 (15)	45.2 (16.9)	23.8 (22.9)	14.5 (18.9)	7.2 (9.2)
MTD + 30% extra	30.6 (26.9)	49.6 (12.6)	29.1 (31.4)	25.1 (31.6)	4.3 (5.6)
OXY	26.2 (22)	45.6 (18)	(1) 18 (17.8) ↓	19.2 (26.6)	4 (6.7)
GPN	29.1 (27.8)	47 (18)	25.6 (28.7)	22.3 (28.4)	7.2 (8.4)
BUPRENORPHINE GROUP					
Control (ref)	14.2 (15.5)	33.2 (25.9)	13.1 (17.1)	13.5 (20.4)	3.8 (8)
BPN +30% extra	15.2 (21.2)	43.7 (20.6)	8.7 (15.8)	10.5 (20.1)	5.4 (9.8)
OXY	20.1 (21.2)	(2) 50.3 (22.6) ↑	23.3 (23.9)	20 (22.5)	(3) 25.5 (23.2) ↑
GPN	28.4 (28.6)	44.4 (19.7)	31.8 (27.6)	24.5 (29.8)	19 (24.2)

(1) Coeff -21.1 (95% CI -36.5, -5.7) P<0.01
(2) Coeff 31.6 (95% CI 10.9, 52.3) P<0.01
(3) Coeff 23.4 (95% CI 0.07, 46.7) P<0.05

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Individual variability – pain tolerance

INDIVIDUAL PAIN TOLERANCE (2hr) Methadone arm

INDIVIDUAL PAIN TOLERANCE (2hr) Buprenorphine arm

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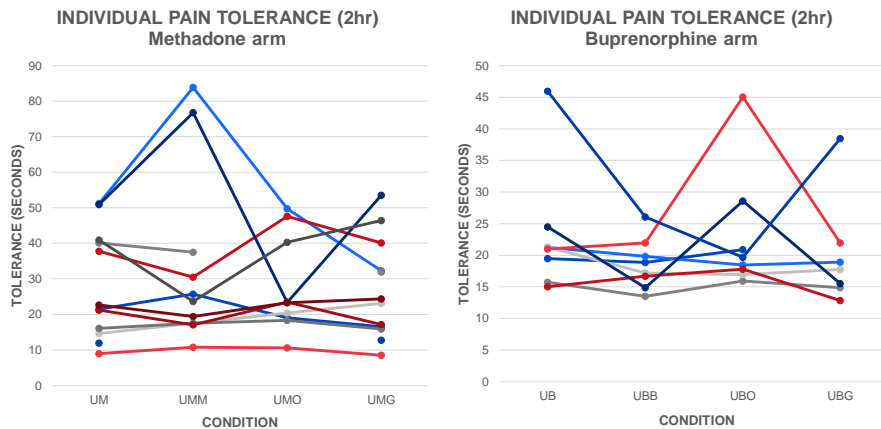
DISCUSSION

- No difference in cold pressor tolerance between experimental conditions
  - Interventions not different to placebo on analgesic effect
  - Less perceived pain in extra 30% methadone arm
  - Trend towards oxycodone effect in buprenorphine arm
- For some conditions, effects driven by 1-2 responders (i.e. larger effect)
  - The same condition didn't work for everyone
  - Nothing worked for most people
- Pain management is complex in these patients

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DISCUSSION

- Drugs were in sufficient doses
  - Doses resulted in psychoactive effects (OXY, MTD + 30%) but little/no analgesia
- There is still no clarity regarding best way to treat acute pain in patients on opioid agonist treatment
  - Further research is needed to explore non-opioid strategies
  - No adverse effects, suggesting that while a trial may not work, it probably will not cause harm
  - Gabapentin did not work for acute pain in this trial

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QUESTIONS

THANK YOU!

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