Short or Long Ketamine infusions – Does it matter?

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Introduction

Although sub-anaesthetic ketamine infusions are an established pain management treatment option, the ideal duration is unknown.

Our study compared the outcomes of eight hour and multiday sub-anaesthetic ketamine infusions in patients attending a general pain clinic.

The day stay procedure allows more predictable admissions, reduces cost, inpatient bed occupancy and inconvenience to patients and families.

Methods

We audited the outcomes of a consecutive series of public and private patients with chronic pain treated with ketamine infusions over a four year period in three hospitals.

We report the average maximum rate and amount of ketamine administered, global perceived effect, changes Brief Pain Inventory and pain self-efficacy scores from baseline at discharge, 1 month, 3 months and 6 months.

Treatment data was entered prospectively into an electronic database (MedquestOzPlus, http://ozmed.com.au:86). Data sets were compared using paired t-tests in Excel 2010 for Windows.

Technique

The 8 hour and multi-day treatments use standardised: protocols. After administering 100mcg clonidine, 2.5 mg diazepam and 10mg metoclopramide the 8 hour infusions start with a 5mg loading dose and 10mg/hour continuous infusion that is adjusted by 2-5mg/h every 15 minutes as needed and tolerated to get pain below 3/10.

The multiday inpatient ketamine infusions receive 50-100mcg clonidine bd, diazepam 2.5mg bd, antiemetics prn and start with a 5mg loading dose, 10mg/hour infusion that is adjusted by 2-5mg/h every 2-4 hours as needed and tolerated to get pain below 3/10.

Quetiapine, lorazepam , extra clonidine or loperimide were administered if needed

Results

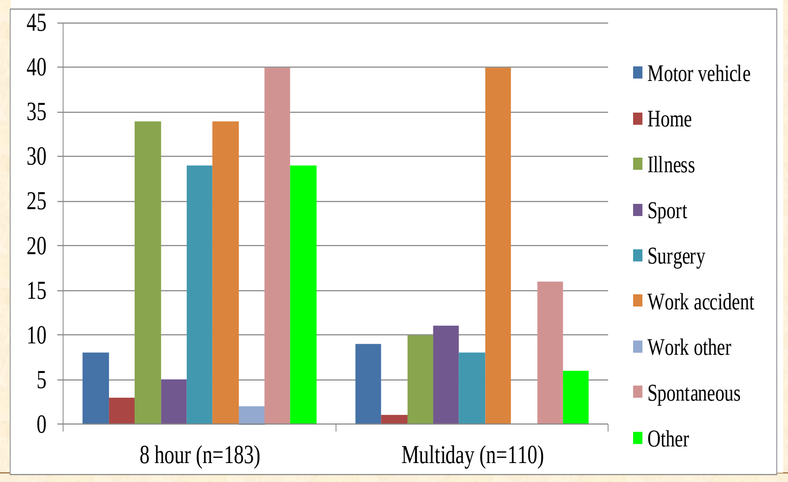
A search of our electronic database found 179 patients who had received one or more ketamine infusions between March 2009 and April 2013.

Of these patients, 100 received “short 8 hour” ketamine infusions and 79 received “multiday” ketamine infusions lasting from 48 to 260 hours.

Greater than 1.5/10 reduction in pain was reported by at least 9, 11 and 9 patients respectively at 1, 3 and 6 months in the short ketamine group. The multiday ketamine group had an average pain duration of 11.9 years. Greater than 1.5/10 reduction in pain was reported by at least 12, 13 and 10 patients respectively at 1, 3 and 6 months in the multiday ketamine group.

There was no significant change in pain self efficacy score at 1, 3 or 6 months in either group from the baseline

Aetiology



Results

Demographics

	N	Age	Male	Female	Weight	Pain Duration
8 hour	100	50	32	68	81.7	9.6y
Multiday	79	52.6	28	51	83.1	12.3y

Ketamine

	Duration Hours (mean)	Max Rate mg/hour	Range mg/hour	Amount Ketamine (mean)	Benefit Days (mean)
8 hour Infusion	7.3 hour (sd 1.0)	43.3 (sd9.9)	15-60	264 (sd76)	50.1 (sd67)
Multiday infusion	144 hour (sd39.2)	30.3 (sd14.1)	5-60	3665 (sd2411)	50.8 (sd67.9)

Satisfaction

	8hour At Discharge	8 hour At Review	Multiday At Discharge	Multiday At Review
Worse	4	1	1	0
No Change	11	14	9	17
Better	85	46	69	31
Unknown	0	39	0	31

Brief Pain Inventory Average Pain Severity

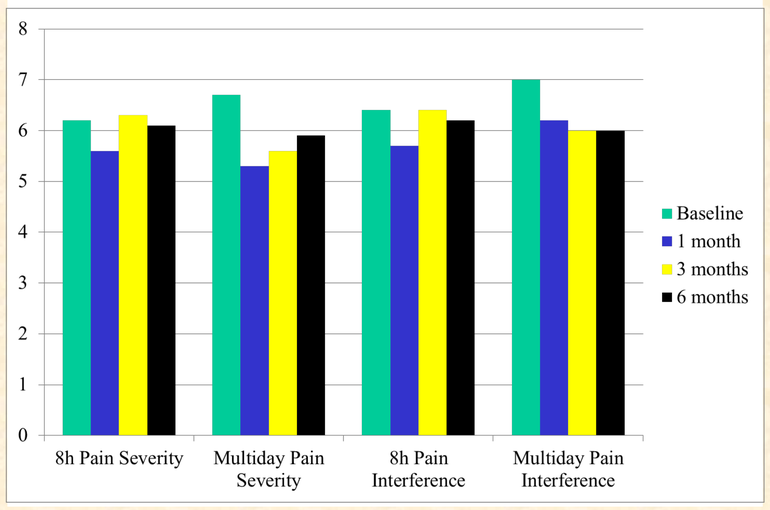
*p<0.05	T0 average	T1m n=35/32	T3m n=62/61	T6m n=41/44
8 hour	6.2	5.6*	6.3	6.1
Multiday	6.7	5.3*	5.6*	5.9*

Brief Pain Inventory Change in Pain Interference

*p<0.05	T0 average	T1m N=67/32	T3m N=120/61	T6m n=89/44
8 hour	6.4	5.7*	6.4	6.2
Multiday	7.0	6.2	6.0*	6.0

Pain Severity and interference

Baseline versus 1, 3 & 6 months



Reported Adverse Events

8h ketamine		Multiday Ketamine	
Very Common > 10%	**%**	**Very Common > 10%**	**%**
Nausea	22	Hallucinations	15
Common 1-10%		**Common 1-10%**	
Hallucinations	7	Confusion	9
Vomiting	4	Injection site pain	5
Confusion	4	Insomnia	5
Headache	3	Nausea	6
Anxious	2	Somnolence	4
Blurred /Double Vision	2	Blurred /Double Vision	4
Paraesthesia	2	Agitation	3
Somnolence	2	Aspiration pneumonia	3
Agitated	1	Dizziness	3
Chest Pain	1	Hypotension	1
Cramps	1	Suicide <3m post Tx	3
Dizziness	1	Cramps	1
Dyspnoea	1	Dyspnoea	1
Fatigue	1	Euphoria/mania	1
Hypertension	1	Fatigue	1
		Hypertension	1
		Restlessness	1
		Weakness	1

Discussion

Between group analysis showed pain reduction at 1m in the inpatient group to be the only significant difference .

There was no difference in duration of benefit between the two groups.

Although improvement in both groups is modest, at least 11% and 16% of the 8h infusions and multiday infusions respectively reported at least 1.5/10 reduction in pain intensity at 3 months

This review shows the effects of both short and multiday ketamine infusions are generally short lived, however responders can often obtain sustained pain relief from repeated short or long infusions.

Further research is required to identify which conditions respond to ketamine and which patients will benefit from periodic maintenance ketamine infusions.

Limitations:

The groups were not equivalent, had different aetiologies, demographics, pain duration and baseline pain scores and the clinical indications for each treatment were different.

8 hour infusions were often used as diagnostic tool to allow reassessment and to reduce sensitisation . Multiday infusions were more often used to reduce sensitisation, more complex patients and as part of an opioid detoxification program

Conclusions

This audit shows the outcomes achieved with short day-stay ketamine infusions in selected patients are not inferior to longer inpatient treatments other than pain relief at 1 month.

Day-stay ketamine infusions have the advantage of reduced hospital stay, cost, social and family disruption and may be a cost effective option in suitable patients.

Reprints

Available on request from: mtaverner@phcn.vic.gov.au

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