Ketamine-Midazolam Anesthesia for intractable Complex Regional Pain Syndrome-Type I (CRPS-I)

Ralph-Thomas Kiefer[1], Peter Rohr[2], Annette Ploppa[1], Hans-Jürgen Dieterich[1], Karl-Heinz Altemeyer[2], John Grothusen[3], Klaus Unertl[1], Robert J Schwartzman[3]

[1]Dept. of Anesthesiology, Eberhard-Karls University, Tuebingen, Germany; [2]Dept. of Anesthesiology, Klinikum Saarbruecken, Germany;
[3]Dept. of Neurology, Drexel- University, Philadelphia, U.S.A.

1210-P126

INTRODUCTION

CRPS-I, a debilitating neuropathic pain state, may be very difficult to treat. The disease may spread and be intractable to standard therapy.[1] More effective therapeutic options are desperately needed.[2] Functional and structural changes in central pain processing neurons (central sensitization) are thought to be important for initiating and maintaining neuropathic pain, of which CRPS-I is a subset. Central sensitization seems to occur in consequence of activity dependent *N*-Methyl-D-Aspartate (NMDA) receptor activation. [3,4] Growing clinical evidence suggests NMDA-antagonists for the therapy of neuropathic pain & CRPS.[5]

METHODS

10 ASA I-II patients (intractable CRPS)
Anesthesia Induction
ketamine (0.5-1mg/kg)
midazolam (2.5-5mg), repetitively
Maintenance (5 days)
Infusions: ketamine (3-7 mg/kg/h) & midazolam (0.15-0.3)
Spontaneous breathing (Pat# 1, 2, 4)
Intubation/Mechanical Ventilation
Patients # 3, 5-10
Emergence (day 6)
slowly tapering of infusions

Summary of patient's characteristics

#	Age	Sex	Initiating Injury	Spread	Duration
1	16	f	sprain & brachial plexus traction injury	non-generalized	8 months
2	28	f	brachial plexus traction injury	non-generalized	1 year
3	24	m	lymph node invasion of brachial plexus	non-generalized	1 year
4	46	f	brachial plexus traction injury	generalized	6 years
5	44	f	crush injury foot	generalized	6 years
6	30	f	electrical shock injury to arm	non-generalized	2 years
7	41	f	traumatic knee injury	non-generalized	2 years
8	28	f	L5-S1 radiculopathy	generalized	6 years
9	19	f	foot # & brachial plexus traction injury	generalized	6 years
10	22	f	traumatic hand injury	generalized	6 years

Table 1: Patient number (#), characteristics, initiating injury, status of spread, and duration of symptoms.

RESULTS

Summary: Results

#	total PR	recurrence of				Low dose ketamine-
	[months]	ONP	Site	NPP	CRPS-relapse	success
1	since 42	no		no	no	
2	since 14	yes	bp	no	no	
3	for 2	yes	rp	no	no	
4	for 2	yes	bp	yes	less severe	not applied
5	for 4	yes	ps	yes	no	yes
6	for 4	yes	bp	yes	no	yes
7	for 2	yes	kp	no	no	no
8	for 1	yes	rp	yes	no	not applied
9	since 2	no		no	no	
10	for 2	yes	bp	no	no	not applied

Table 2: Results: Patient #, duration of total pain relief (PR), recurrence of original nociceptive pain (ONP), site (bp:brachial plexus, rp: radicular back pain; ps: pseudoarthrotic pain, kp:knee pain); recurrence of neuropathic pathological pain (NPP) features (hyperalgesia, allodynia), CRPS-relapse &severity and success of ketamine retreatment (low-dose outpatient).

Initial Observations

Immediate treatment response
- total pain relief (10/10)
- no hyperalgesia, no allodynia (10/10)
- absence of CRPS-I-signs (10/10)

Adverse Treatment Effects
- slight psychomimetic effects up to 3 months (3/10)
- urinary infection (2/10)
- respiratory infection (5/10)
- weaning problems (obesity) (1/10)

Long-Term Observations

Lasting full pain relief (pathological)
- since 3.5 years (# 1)
- since 14 months (# 2)
- since 5 months (# 7, 8)
- since 2 months (# 9)

Recurring original nociceptive pain
- after 6-8 weeks (8/10)
- at original injury site (7/8)

Recurrence of pathological pain
- hyperalgesia/allodynia (4/10)
- ketamine-retreatment (3/4)
  - treatment success (2/3)

CRPS-relaps (1/10) (#4,less severe)

Consumption of Analgesics
- Significant reduction (exept #4)

Social/Professional Reintegration
- full in (5/10)
- improved (3/10)
- no improvement (2/10)

Fulminant CRPS-I & full recovery after ketamine-midazolam anesthesia (since >3.5 years)

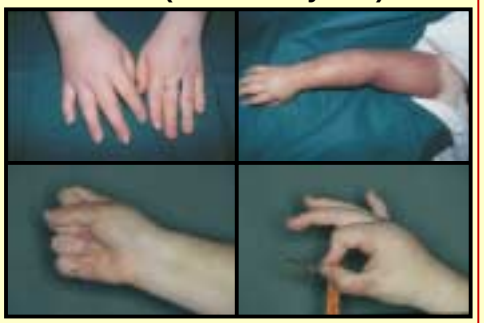

Figure 1: Clinical Course of the most dramatic case (#1). Upper row: left: at admission (CRPS-I right hand); right: fulminant exacerbation of symptoms, clinical failure of standard therapy. Lower row: left/ right: functional outcome 1 week after ketamine-midazolam anesthesia. Total recovery since 3.5 years.

CONCLUSIONS

Ketamine-midazolam anesthesia shows promise as potentially effective therapeutic option for severe and otherwise intratable CRPS-I

CHALLENGES

- **Which patients benefit most?**
- **Patient selection criteria?**
- **Best Timing (stages)?**
- **Dose-Response Curves?**
- **Maintenance Strategies?**

References: 1. Maleki J et al. Pain 2000; **2.** Schwartzman RJ. N Engl J Med 2001; **3.** Woolf CJ, Salter MW. Science 2000; **4.** Schwartzman RJ et al. Arch Neurol 2001; **5.** Sang CN, J Pain Symptom Manag 2000