Bilaga till SBU-kommentar

Ketamin vid svårbehandlad depression, rapport 2017_01 (2017)

Bilaga 1 Referenser till inkluderade ketaminstudier i översikterna

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TABLE 1. Characteristics of included ketamine studies

Study	Study design	Diagnosis Duration of illness (mean, years); Duration of episode (mean, months)	Baseline severity Ketamine vs Control (mean (SD or)); [Inlusion criteria]	N	Treat-ment	Control	Treatment (Tx) strategy; Dose (mg/kg)	Concomitant treatment	Follow-up (hours)	Outcomes*	Risk of bias* Comments
Caddy et al: DEPRESSION											
Ketamine vs Placebo											
Berman 2000 USA	RCT DB, crossover	MDE (1 BD-dep); Duration of illness or episode NR	HDRS 33,0 (6,7); HDRS 26,9 (5,8)	9	5 ketamine	4 placebo	**Monotherapy:** 2w drug free# prior Tx 0,5mg/kg i.v.	None	24h, 48h, 72h	Response rate (>50% HDRS); (BDI, BPRS, VAS)	High to Unclear risk of bias; Adverse events reported: BPRS - positive symptoms/ psychotomimetic effects; VAS - intoxication high.
Zarate 2006, USA	RCT DB, crossover, 1w apart	MDD; TRD; 24 y illness, 34 mo episode	HDRS 24,89; HDRS 24,44 [HDRS > 18]	18	9 ketamine	9 placebo	**Monotherapy:** 2w drug free# prior Tx 0,5mg/kg i.v.	None	24h, 48h, 72h, 1w	Response rate (>50% HDRS); Remission rate (≤7 HDRS); (BDI, BPRS, YMRS, VAS)	Low to Unclear risk of bias. Adverse events reported: BPRS - positive symptoms YMRS - mania
Sos 2013, Czech Republic	RCT DB, crossover	MDD hospitalized; 10 y illness, 11 mo episode	MADRS 20,4 (4,7); MADRS 24,6 (4,8) [MADRS > 20]	30	11 ketamine	19 placebo	**Add-on:** 3w stable on medication prior Tx; 0,5mg/kg i.v.	Existing medications	24h, 72h, (96h), 1w	Response rate (>50% MADRS); (BPRS)	Low to Unclear risk of bias. Objective: Link between anti-depressant and psychoto-mimetic effects (BPRS). Adverse events NR.
Järventausta 2013, Finland	RCT DB	MDD (severe/ psychotic); TRD; Duration of illness or episode NR	MADRS 36,9; MADRS 37,3	32	16 S-ketamine	16 placebo	**Add-on:** Ketamine as adjuvant during ECT; 0,5mg/kg i.v.	**ECT**; Existing medications;	1w, 5 ECT ses-sions	Response rate (>50% MADRS); Remission rate (≤7 MADRS); (BDI)	Low to Unclear risk of bias; Objective: Ketamine as anaesthtic adjuvant during ECT. Adverse events NR.
Loo 2012, Australia	RCT DB, parallell	MDE (9 BD-dep); TRD; 36-53 w episode	MADRS 32,1 (4,5); MADRS 32,7 (7,9)	51	26 ketamine	25 placebo	**Add-on:** Ketamine as augmentation to ECT; 0,5mg/kg i.v.	**ECT** 3x/w; Existing medications;	1w, 2w, (1mo); 6 ECT ses-sions	Response rate (>50% MADRS); Remission rate (≤10 MADRS); MADRS	Low to high; Objective: Neuro-psychological outcomes. Adverse events reported: psychotomimetic, mania/ hypomania.
Ketamine vs Active control											
Murrough 2013 USA	RCT DB, parallell	MDD; TRD; 20-24 y duration 146-109 mo index episode	MADRS 32,6 (6,1); MADRS 31,1 (5,6); [IDS-C > 32]	73	47 ketamine	25 mida-zolam	**Monotherapy** Drug free# 0,5mg/kg i.v.	hypnotic (non-benzidia-zepine)	24h, 72h, 1w	Response rate (>50% MADRS); MADRS; BPRS	Low to Unclear risk of bias. Adverse events reported, incl: dissociative, psychotic symptoms.
Yoosefi 2014, Iran	RCT DB	MDD Duration of illness or episode NR	HAM-D 23,60; HAM-D 22,86 [HAMD >18]	31	17 ketamine	14 thio-penthal	**Add-on:** Ketamine as adjuvant during ECT; 0,5mg/kg i.v.	**ECT** (randomized after ECT 3x/w for 2w)	72h, 2w, 4w	Response rate (>60% HAMD); HAMD, MMSE,	Low to High risk of bias. Objective: Ketamine as induction agent for anaesthesia. Protocol unclear. Adverse events reported: MMSE - Cognition/memory
Ghasemi 2013, Iran	RCT SB	MDD, in MDE* (1 BD, 5 GAD/OCD, 4 personality dis, 1 addiction) 9 w episode	HRSD 30,22 (5,78); HRSD 35,88 (6,47)	18	9 ketamine	9 **ECT** + thiopent hal	**Unclear.** 1w infusion: 0,5mg/kg over 45min; every 48h	Existing medications;	24h, 72h, 1w, 2w	Response rate (>50% HDRS); HRSD, BDI	Low to Unclear risk of bias. Protocol unclear. Ketamine "3 infusions on 3 test days every 48h". Adverse effects reported: hemodynamic.
McCloud et al: BIPOLAR depression											
Diazgranados 2010 USA	RCT DB crossover, 2w apart	BD I or II with depression; MDE > 4w; TR > 1; 28 y illness; 15 mo episode	MADRS 31,2 (4,4); MADRS 33,9 (4,8) [MADRS > 20]	18	9 ketamine	9 placebo	**Add-on:** 2w drug-free# 0,5mg/kg i.v.	Lithium or valproate	24h, 48h, 72h, 1w, 10d, 2w	Response rate (50% MADRS); Remission rate (MADRS<10); (HDRD, HARS, BDI, BPRS, YMRS, CADS)	Low to Unclear risk of bias. Adverse events reported.
Zarate 2012 USA	RCT DB, crossover	BD I or II with depression; without psychotic features; MDE for 4w	MADRS? 34,1 (5,4); MADRS 35,6 (5,8) [MADRS > 19]	15	7 ketamine	8 placebo	**Add-on:** 2w drug-free# 0,5mg/kg i.v.	Litium or Valproate	24h, 72h, 1w, 2w	Response rate (50% MADRS); Remission rate (MADRS<10); MADRS, HRSD, BDI, BPRS, YMRS, other	Low to Unclear risk of bias. Adverse events reported.

Diagnoses : MDD - Major Depressive Disorder; MDE - Major Depressive Episode; BD - Bipolar Disorder; TRD - Treatment Resistant Depression;
GAD - Generalized Anxiety Disorder; OCD - Obsessive Compulsive Disorder

Depression rating scales : MADRS - Montgomery - Åsberg Depression Rating Scale; HDRS - Hamilton Depression Rating Scale; BDI - Beck Depression Inventory

Other rating scales : BPRS - Brief Psychiatric Rating Scale - positive symptoms; VAS - Visual analog scale (for intoxication); YMRS - Young Mania Rating Scale (for mania)
HARS - Hamilton Anxiety Rating Scale; CADS - Clinician Administered Rating Scale;

Outcomes* As defined by original authors and used in the meta-analyses of the systematic review

Drug free# - Free from other antidepressant/ psychotropic medication. Other drugs may be permitted (hypnotic, anaesthetic/analgesic/muscle relaxant)

Risk of bias*- Assessed and reported by authors of the systematic review. Itemized risk of bias, no overall assessment was made