Opiate Prescribing in the Elderly: A Systematic Review

Melissa Jassal, B.Sc.(Pharm); Karen Dahri, BSc., BSc(Pharm)., PharmD., ACPR.; Greg Egan, BSc(Pharm)., PharmD., ACPR.

Background

- In 2010, ~25% of elderly Canadians reported experiencing chronic pain. This number is projected to rise as the average age of the population increases
- Opiates often necessary for the treatment of chronic pain in the elderly
- Evidence-based recommendations for age-adjusted dosing of opiates are currently lacking

Objectives

- To characterize the literature describing the therapeutic use of opiates in the elderly
- To inform an algorithm for prescribing opiates in the elderly population at VGH

Methods

- Population: Patients > 65 years old with persistent pain and receiving opiates (codeine combination products, oxycodone, hydromorphone, morphine, methadone, buprenorphine, fentanyl and sufentanil)
- Inclusion: Observational studies, population-based cohort studies, retrospective analyses and control trials
- Exclusion: Narrative reviews, editorials, acute or post-operative pain, animal studies, languages other than English
- Data Collection: Descriptive data including type of opiate used, dosing of opiate, comorbidities, etiology of pain, pharmacokinetic parameters, drug interactions and adverse effects
- Search: Electronic databases EMBASE and MEDLINE from January 1990 to present. Search terms included: opioid/narcotic analgesic, opiate* or opioid, elder* or senior* or geriatric* or older adult* or frail*, chronic pain or persistent pain
- Assessment of bias: Cochrane Risk of Bias and Risk of Bias in Non-randomized Studies of Interventions (ROBINS-1) tools applied
- All studies were reviewed in duplicate. Any discrepancies were resolved by a third reviewer

Results

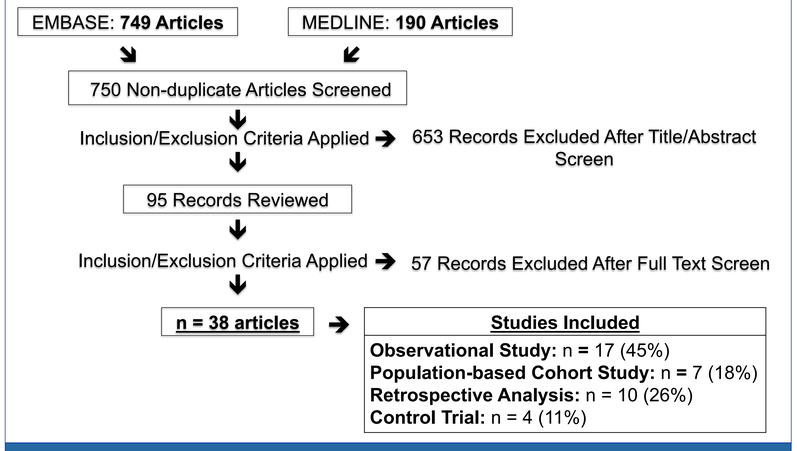

Figure 1: PRISMA Flow Diagram for Systematic Review

Table 1. Summary of Control Trials & Outcomes

Author	Design	N	Mean Age	Intervention	Control	Population Characteristics (incidence)	Efficacy Outcomes		ADE (incidence)
Brevik, 2010	PC, DB, RCT	100	62.9	BTDS 5 – 20 ug/h	Placebo	• **Etiology of Pain:** Osteoarthritis (100%)	• **WOMAC OA (index of hip and knee pain)**	• NSS	Dizziness (25%), Constipation (24%), nausea (37%), vomiting (16%) Pruritus (61%)
Likar, 2008	OL	30	74.3	BTDS at doses 35, 40 and 50 ug/h	No control	• **Etiology of pain:** MSK causes (63%), neuropathy (13%), cancer (6.5%) • **Comorbidities:** Cardiovascular disease (80%)	• **VAS** • **NRS**	• NSS • NSS	Dizziness (53.3%), malaise (30%) nausea (40%), constipation (30%), vomiting (16.7%) Pruritus (20%)
Rauck 1994	DB, RCT	156	72	Codeine 30 – 60mg/ acetaminophen 300 – 600 mg q 4 – 6h prn	Tramadol 50 – 100mg po q 4 – 6h prn (max: 400mg/24h)	• **Etiology of pain** Arthritis (72%), back/neck pain (14%), neuropathy (7%),	• **Pain intensity score**	• NSS	Dizziness (4.5%), Constipation (9.6%), nausea (4.5%)
Kjaersgaard-Andersen, 1990	DB, RCT	158	66	Codeine 60mg/ paracetamol 1000mg	Paracetamol 1000mg po TID	• **Etiology of pain:** Arthritis (100%)	• **Pain intensity score**	• p < 0.01 for codeine/ paracetamol group	Dizziness (3%), somnolence (20.3%) Constipation (36.1%), nausea (32.3%), vomiting (14.6%),

ADE: adverse event, **PC:** placebo controlled, **DB:** double blind **RCT:** randomized control trial, **OL:** open-label, **BTDS:** buprenorphine transdermal patch, **WOMAC**: Western Ontario and McMaster Universities Arthritis Index, **VAS:** visual analog scale, **NRS:** numerical rating scale

Table 2: Cochrane Risk of Bias for Control Trials

Domain	Brevik, 2010	Likar, 2008	Rauck, 1994	Kjaersgaard-Andersen, 1990
Random sequence generation				
Allocation concealment				
Blinding of participants & personnel				
Blinding of outcome				
Incomplete outcome data				
Selective outcome data				

Low Risk of Bias | Unclear Risk of Bias | High Risk of Bias

Table 3. ROBINS-I tool for Non-Randomized Studies

Domain	Low	Moderate	Serious	Critical	No Information
Bias Due to Confounding	4	4	12	6	7
Bias Due to Selection	28	3	3	0	0
Bias Due to Classification	21	5	8	0	0
Bias Due to Deviations	24	6	0	0	4
Bias Due to Missing Data	25	3	2	0	4
Bias Due to Measurement of Outcomes	10	3	21	0	0
Bias Due to Selection of the Reported Result	6	13	3	0	2

Discussion

- 19 studies (50%) reported on comorbidities; common ones including cardiovascular disease, renal impairment and dementia/cognitive impairment
- Most studied opiates were morphine, codeine products, and oxycodone (47%)
- In the last 10 years, transdermal buprenorphine and oxycodone/naloxone were more frequently studied
- CNS side effects (dizziness, somnolence, fatigue) were the most commonly seen adverse effects (6.7% of patients)
- Very low incidence of respiratory depression overall (1 patient)

Limitations

- None of the studies assessed pharmacokinetic parameters or drug interactions
- Majority of studies did not evaluate dosing
- Only half included patient comorbidities
- Overall there is a large amount of heterogeneity in the data limiting our ability to draw conclusions

Conclusions

- More higher quality evidence is required to understand the therapeutic use of opiates in the elderly population
- Due to the poor quality of data found; unable to use the results of this review to inform an algorithm for prescribing opiates in the elderly
- Imperative to continue considering patient-specific parameters when prescribing and dosing opiates in this population

Acknowledgments

- Many thanks to Hans Haag (BSc.) for his role in data collection during this project.