Do patients with cancer pain achieve complete pain relief from opioid therapy? Results of a systematic literature review

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Introduction

Opioids are considered the mainstay of treatment for moderate to severe cancer pain.[1,2] Cancer patients are encouraged to titrate opioid analgesics to become pain-free, or until side-effects limit additional dosing.[3] In a study looking at opioid therapy for cancer pain, patients received fentanyl transdermal along with unlimited oral morphine for breakthrough pain.[4] Despite unlimited availability to opioids, patients did not titrate themselves lower than pain scores of 30/100 on a visual analog scale.[4] This suggests that, on average, patients are not achieving pain free status. It is unclear whether these results are study specific, or represent a more general phenomenon in which cancer patients do not achieve complete pain relief from opioid therapy.

The **aim** of investigation was to systematically review all published opioid trials in cancer pain patients to assess patient pain scores and determine if pain free status was achieved in the majority of patients.

Methods

A digital review of the English language scientific literature encompassed all published papers to January, 2015. This database search included PubMed and generalized Internet search. Keywords searched included: cancer pain, opioids, pain scores, and analgesia; which produced 905 potential papers. Each title was then reviewed for a clinical trial of opioid therapy for cancer pain, resulting in 180 possible papers. These papers were then reviewed by all authors yielding 58 papers meeting inclusion criteria. Inclusion criteria included opioid therapy, cancer pain, clinical trial, and pain scores (NPS,VAS only). Exclusion criteria included non-malignant pain, inappropriate pain measures (Likert, Faces scale, observer rating, categorical), and studies in which patients did not have unlimited access to PRN opioids. Finally, all references of the included 58 papers were reviewed for completeness. This added 42 potential papers focusing on opioids in cancer pain. Careful study of the 42 additional papers added only 4 additional papers which met inclusion criteria.

The primary outcome measures were VAS or NPS pain scores before and after treatment intervention. Additional data collected was gender, age, opioid type and dose, levels of patient satisfaction and types of studies.

Table 1: Raw data for each eligible cancer pain clinical trial

Study	# of Patients	Study Duration (days)	Age	Males	Females	Initial Pain Score	Ending Pain Score
Apolone G	257	84	64	63	164	6.4	2.5
Arkinstall WW	17	20	63	12	5	1.5	1.4
Babul N	22	7	55	9	13	2.5	2.4
Bruera	22	7				3.0	2.8
Baek SK	318	56	59	199	119	5.5	4.3
Boureau F	52	7	62	34	18	3.1	3.0
Brema F	131	180	59	86	45	7.0	3.5
Bruera E	6	86	61	3	3	2.4	2.7
Bruera E	23	8	64	12	10	1.6	1.2
Bruera E	103	28	60	37	66	7.8	3.0
Dale O	19	7	57	11	8	1.9	0.4
Deschamps M	20	14	57	13	7	1.3	1.5
Dhaliwal HS	30	14	64	17	13	2.3	1.7
Forman WB	69	33	61	45	24	3.5	1.5
Grond S	50	535	57	38	12	4.5	1.5
Hagen NA	31	14	56	13	18	2.9	2.6
Hagen NA	25	14	53	12	13	1.9	1.9
Han HS	878	57	63	537	341	5.7	3.1
Hanks GW	18	7	70	7	11	8.3	7.9
Hays H	45	7	57	19	26	2.0	1.9
Heiskanen T	20	3	63	9	11	3.2	3.3
Klepstad	40	7	64	22	18	5.9	2.4
Koizumi W	20	84	69	19	3	4.8	1.6
Komurcu S	99	28	55	41	58	6.3	3.0
Korte W	20	28				5.3	2.5
Leppert W	30	14	70	11	19	6.0	2.4
Levy MH	6	55	66			4.4	2.3
Lundorff L	18	26	64	8	10	4.0	2.5
Marinangeli F	92	3269	63	56	43	4.1	
Maves TJ	10	28	57.7	6	4	5.1	5.0
Moksnes	41	14	59	22	19	4.6	3.8
Melilli G	42	90	72	19	23	8.0	3.0
Mercadante S	60	7	66	44	36	7.0	2.8
Mercadante S	50	28	66	20	30	5.9	1.7
Mercadante S	50	28	64	32	32	6.4	3.0
Mercadante S	46	84	63	19	27	7.2	1.6
Mercadante S	39	28	67	22	17	6.4	3.2
Mercadante S	70	28	59	363	34	7.5	2.8
Mignault GG	19	5	57	9	10	5.5	5.7
Miyazaki T	85	12	66.5	45	40	1.9	1.7
Moolenaar F	20	10	59	15	5	2.1	2.0
Mystakidou K	130	56	62	73	57	5.9	0.8
Mystakidou K	113	42	61	54	59	7.1	1.0
O'Brien T	69	21	64.3			1.5	1.5
Pace MC	52	56	54.5	27	25	6.5	4.5
Pan H	216	28	57	90	90	7.1	1.8
Poulain P	289	28	63	124	165	3.8	1.5
Rhondali W	19	14	55	12	7	6.0	3.0
Ridgway D	38	28	57	24	14	2.5	2.5
Silvestri B	390	21	66	216	174	7.2	2.1
Sima L	246	4	61	60	60	5.2	4.8
Slatkin NE	80	364	57	39	41	3.0	3.5
Sloan P	86	14	53.5	33	53	2.8	3.2
Sloan PA	53	84	61	26	27	2.8	2.8
Slover R	5	28	44.6	4	1	6.4	2.9
Stambaugh JE	30	28	60	10	20	6.0	2.2
Suzuki T	37	6	53	0	37	5.8	2.6
Tawfik M	292	28	56	131	161	5.8	3.3
Vielvoye-Kerkmeer AP	28	28				5.0	3.2
Walsh TD	33	6	60	15	12		2.2
Watanabe S	12		60	8	3		2.7
Zech	20	7	60	10	10	7.0	3.0
TOTAL PATIENTS	5251						

Results

The English published literature revealed 62 papers of eligible trials of opioid therapy for the treatment of cancer pain (Table 1). A total of 5,251 patients were counted across all studies. The weighted mean pain score at the start of opioid therapy across all studies was 5.4 (0=no pain; 10=worst possible pain), and the weighted mean pain score at the end of the trials was 2.7.

Conclusions

Cancer patients with chronic pain do not titrate themselves to 0/10 relief despite unlimited access to opioids, and in spite of the stated goal of opioid therapy being complete pain relief.

The mean pain score for patients treated for cancer pain is close to the moderate-severe rating, higher than what healthcare providers would suggest is possible and recommended.

The reasons that cancer patients do not titrate themselves to lower pain scores remains unclear and will require further investigation. The authors hypothesize that patients are balancing analgesia with unwanted opioid adverse effects yielding a final pain score much greater than 0 or 1/10, the goal of cancer pain therapy.

References

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