Comparing opioids:

A guide to estimating oral morphine equivalents (OME) in research

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NDARC Technical Report No. 329

Recommended citation: Nielsen, S., Degenhardt, L., Hoban, B. and Gisev, N.(2014). *Comparing opioids: A guide to estimating oral morphine equivalents (OME) in research*. Technical Report No. 329 Sydney: National Drug and Alcohol Research Centre, University of NSW.

ISBN: 978-0-7334-3482-2

Background

Opioids are widely used for providing analgesia for acute and chronic pain, including cancer pain. Global use of opioids has risen dramatically since the early 2000s [1], with the highest levels of opioid consumption accounted for by use in high income countries such as the United States, Canada and Australia[2]. In many countries there have been well-documented increases in morbidity and mortality associated with the increased use of opioids[3-9], which has led to a need to gain a deeper understanding of the manner in which opioids are used and changing patterns of use. Further, with increasing availability of different opioids and different formulations, understanding opioid use at the population level has become increasingly complex.

This growing research area examining pharmaceutical opioid use has led to a need to develop clear ways to represent and compare opioid use. For drug utilisation in particular, there is a need to present usage data consistently, taking into account dosing requirements. One method of representing opioid use at the population level is through the application of Defined Daily Doses (DDD). However, representing opioid use as DDDs may not optimally represent clinical dosing of opioids[10], partly because opioids require highly individualised dosing and need to be titrated to pain response, rather than having standard therapeutic dose ranges.

An alternate way to represent opioid use and address the limitations of using DDDs, is through the application of oral morphine equivalents (OMEs). Oral morphine equivalents are based on the idea that different doses of different opioids may give a similar analgesic effect. Where the

doses of two different opioids are considered to give a comparable analgesic effect, they are deemed to be *equianalgesic doses*.

Equianalgesic doses of opioids were initially developed using data from studies of acute opioid dosing in opioids naïve participants[10, 11], limiting their relevance to use of opioids for chronic pain, the indication representing the majority of opioid consumption today. Further, there are now a large number of dose conversion tables available and conversion factors vary widely. Combined with multiple patient-related factors to consider when converting doses, there is the potential to calculate very different results for the same patient's dose [11]. This has led to different groups and hospitals developing their own guidelines to take into account clinical experience, and new research reporting conversions with chronic opioid use[12].

From a research perspective, it is important to have a comprehensive resource which will enable comparisons between opioid use in different geographic locations and between populations over different time points. Currently, available tables do not cover the full range of opioids used in Australia, and international references appear to report only a limited number of opioids used in Australia. For this reason, we sought to develop a comprehensive dose conversion table, and report a transparent methodology to support the conversion used. As most of the published literature and guidelines report doses in OMEs, we have compiled a reference that represents a broad range of opioids with simple conversion factors to facilitate representing doses of a wide range of opioids in OMEs.

Methods

A table for converting opioids into OMEs was initially created using leading clinical references in Australia: the Therapeutic Guidelines[13], the Australian Medicines Handbook[14] and a consensus document developed by the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists (FPMANZCA) 2014. Conversions were mostly consistent across references. Where conversion factors were available from multiple sources, the most commonly occurring value was used to establish the final conversion factor. In the case of methadone, which is rarely reported in clinical conversion tables, conversion factors were adapted from Walker et al. [15]. To ensure that the conversion factors reported were consistent with international recommendations, we then examined conversion rates published in national prescribing guidelines or by organisations in Canada, the United Kingdom, the United States and Europe, representing some of the highest opioid consuming regions in the world. Finally, we examined a systematic literature review of chronic opioid dosing studies[12]. While wide ranges were reported in this review, reflecting normal clinical variation, the conversion factors we have chosen to use are within the reported ranges.

Table 1: Conversion factors from Australian sources

		ANZCA guidelines[16]	eTherapeutic Guidelines[17]	Australian Medicines Handbook[18]	Other sources	Recommended OME Conversion factor
ORAL PREPARATIONS						
Swallowed						
morphine	mg/day	1	1	1		**1**
oxycodone	mg/day	1.5	1.5	1.5 - 2		**1.5**
hydromorphone	mg/day	5	5-6.7	4-5		**5**
codeine	mg/day	0.13	0.13	0.15		**0.13**
dextropropoxyphene	mg/day	0.1	not listed	not listed		**0.1**
tramadol	mg/day	0.2	0.2	0.2		**0.2**
tapentadol	mg/day	0.4	not listed	not listed	0.36[19]	**0.4**
methadone	mg/day	not listed	not listed	not listed	4.7[20]	**4.7**
Buccal/Sublingual						
buprenorphine	mg/day	40	37.5	37.5		**37.5**
fentanyl	mcg/day	0.1	not listed	not listed		**0.1**
sufentanil	mcg/day	0.5	not listed	not listed		**0.5**
TRANSDERMALPREPARATIONS						
buprenorphine	mcg/hr	2	2.5	not listed		**2.5**
fentanyl	mcg/hr	3	2.5 - 5 (12mcg/hr) 2.4 - 4 (25-100mcg/hr)	not listed		**3**
PARENTERAL PREPARATIONS						
morphine (sc, iv)	mg/day	3	3	3		**3**
oxycodone (sc, iv)	mg/day	3	3	not listed		**3**
hydromorphone (sc,iv)	mg/day	15	15-20	15-20		**15**
codeine (sc, iv)	mg/day	0.25	not listed	not listed		**0.25**
pethidine (iv, im)	mg/day	0.4	not listed	0.3 - 0.4		**0.4**
fentanyl (iv,im,sc)	mcg/day	0.2	0.15 - 0.2	0.2 - 0.3		**0.2**
sufentanil (iv, sc)	mcg/day	2	not listed	not listed		**2**
methadone (iv)	mg/day	not listed	not listed	not listed	13.5[20]	**13.5**
buprenorphine (im, iv)	mg/day	not listed	75	75		**75**
RECTAL PREPARATIONS						
oxycodone	mg/day	1.5	not listed	not listed		**1.5**

iv = intravenous; sc= subcutaneous; im = intramuscular.

Note: for eTherapeutic Guidelines, Tables 1.14, 1.8, and 10.9 were used.

Table 2. Comparison of recommended OME conversion factor with those recommended by key international sources

		Australia	United Kingdom		United States	Canada	Europe
		Recommended research OME Conversion factor	British National Formulary 66[21]	UKMi[22]	Lexicomp Drug Information Handbook[23]	National Opioid Use Guideline Group[24]	European Association for Palliative Care[25]
ORAL PREPARATIONS							
Swallowed							
morphine	mg/day	**1**			1		1
oxycodone	mg/day	**1.5**	1.5	1.3-2	1-2	1.5	1.5
hydromorphone	mg/day	**5**	5	3.5-10	4	5	
codeine	mg/day	**0.13**	0.1	0.08-0.15		0.15	
dextropropoxyphene	mg/day	**0.1**					
tramadol	mg/day	**0.2**		0.1-0.25			
tapentadol	mg/day	**0.4**		0.3-0.4			
methadone	mg/day	**4.7**					
Buccal/Sublingual							
buprenorphine	mg/day	**37.5**		30-80*			
fentanyl	mcg/day	**0.1**					
sufentanil	mcg/day	**0.5**					
TRANSDERMAL PREPARATIONS							
buprenorphine	mcg/hr	**2.5**					1.7
fentanyl	mcg/hr	**3**					2.4
PARENTERAL PREPARATIONS							
morphine (sc, iv)	mg/day	**3**	2		3		
oxycodone (sc, iv)	mg/day	**3**					
hydromorphone (sc,iv)	mg/day	**15**			20		
codeine (sc, iv)	mg/day	**0.25**					
pethidine (iv, im)	mg/day	**0.4**					
fentanyl (iv,im,sc)	mcg/day	**0.2**			0.3		
sufentanil (iv, sc)	mcg/day	**2**					
methadone (iv)	mg/day	**13.5**					
buprenorphine (im, iv)	mg/day	**75**			75		
RECTAL PREPARATIONS							
oxycodone	mg/day	**1.5**					

Considerations when using OMEs for research purposes

There are some considerations and caveats when using these conversion factors:

- Firstly, these conversion factors are based on clinical guidelines for chronic opioid dosing, including use in both chronic pain and palliative care, which represents the majority of all opioid prescribing. Consequently, conversion factors may differ for acute dosing.
- Many guidelines do not publish conversion rates for methadone, or publish conservative rates due to concerns about incomplete cross tolerance or opioid toxicity with long-acting opioids. As such we have based on our conversion based on published transfers in the direction of methadone to morphine.
- Although ranges are typically reported for dose conversion for some opioids, we have included a single conversion factor, which generally represents a midpoint or modal value of available conversion factors to enable calculation of specific doses. In reality, large ranges exist for dose conversion, representing normal inter-patient variation.
- Where combination analgesics are used, we have only considered the opioid ingredient in the conversion factor as our goal is to represent only opioid use/consumption rather than equipotent analgesic effect of both ingredients in a combination product.
- Our conversion factors are intended to calculate conversions from other opioids to OMEs. Different conversions may be suggested if converting to opioids other than morphine, as conversion rates vary based on the direction of the conversion.
- Finally, concerns about opioid tolerance and potential toxicity, inter-individual variation, concomitant medication use and interactions, renal and hepatic impairment, are just a few of

the many reasons why in clinical practice changing between opioids must be carefully titrated on an individual basis, with conversion tables at best offering a guide as to potential requirements, as opposed to a suggested dose.

For the reasons listed above, these OMEs should not be taken as being suggested for use for clinical purposes. The reader is directed to many of the references consulted in compiling this table for clinical recommendations on dose conversions.

Conclusions

These OMEs provided are a comprehensive document reflecting opioids currently used in Australia. These conversion factors are currently being used in studies estimating opioid use at a population level, and examining changes in opioid use over time.

Acknowledgements

We would like to thank Professor Milton Cohen and Associate Professor Nicholas Lintzeris for providing feedback on the development of this work.

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