CHAPTER 9

Lagniappe: A Little Something Extra in Conversion Calculations

INTRODUCTION

What a crazy ride it's been through eight chapters—switching from one route of administration or dosage formulation using the same opioid, converting between opioids regardless of route or pharmaceutical formulation, dosage titrations, solution calculations, and more. What could possibly be left to talk about? Well, there's always room for dessert! So, what the heck is *Lagniappe* (pronounced *lan-yap*)? Of Louisiana French origin, it means "something given as a bonus or gratuity."[1] Okay, it's not a beignet, but it IS a bonus chapter!

OBJECTIVES

After reading this chapter and completing all practice problems, the participant will be able to:

1. Describe the relative potency of the fentanyl derivatives (alfentanil, sufentanil, and remifentanil), levorphanol, and nalbuphine to more traditional opioids.
2. Given a scenario that results from an opioid conversion miscalculation, analyze the situation and suggest an alternate strategy to improve therapeutic outcomes.

There are two important happenings in this chapter:

1. A review of the lesser-used opioids (the fentanyl cousins [alfentanil, remifentanil, and sufentanil], nalbuphine, and levorphanol)
2. A baker's dozen of the most common mistakes made in opioid conversion calculations (present company excepted)

Those of you who bought this book for staff development purposes can use the mistake examples to stump YOUR chumps!

ISLAND OF ORPHAN OPIOIDS

The Fentanyl Backup Singers—Alfentanil, Sufentanil, and Remifentanil

Fentanyl, alfentanil, sufentanil, and remifentanil are synthetic mu-opioid agonists that are 4-anilidopiperidine derivatives.[2] These agents are widely used as primary anesthetic agents, or more commonly as sedatives and to supplement general anesthesia, as well as several other special situations (e.g., electroconvulsive therapy, carotid endarterectomy, craniotomy).[3] In addition to intravenous (IV) delivery, the fentanyl(s) have been given by other routes including epidural, intrathecal, transdermal, and transmucosal.

Pharmacokinetics and pharmacodynamics

Fentanyl and sufentanil undergo phase I metabolism (oxidative N-dealkylation via cytochrome P450 [CYP3A4]). Sufentanil also undergoes O-demethylation and aromatic

hydroxylation with sufentanil.[2] Alfentanil is primarily metabolized by the cytochrome P450 (CYP) system (CYP3A4 and CYP3A3), and remifentanil is rapidly metabolized by blood and tissue esterases, and to a minor degree, by N-dealkylation.[2] The pharmacological and physiochemical properties of fentanyl, sufentanil, alfentanil, and remifentanil are shown in Table 9-1.[4] Alfentanil has the shortest time to onset and peak effect,

Table 9-1
Overview of Pharmacological Properties of Fentanyl and Its Derivatives[8–19]

	Fentanyl[8,10–18]	Sufentanil[6,8,11–14,16–18]	Alfentanil[7,8,11–14,19]	Remifentanil[8,9,11–14,16–18]
Potency compared with morphine	100–300	800–1,000	40–50	100–200
IV induction dose (mcg/kg)	2–6	0.25–2.0	25–100	1–2
IV maintenance dose (mcg/kg)	0.5–2	2.5–10	5–10	0.1–1.0
IV infusion rate (mcg/kg/hr)	0.5–5	0.5–1.5	30–120	0.1–1.0
Other routes of administration than IV	Transdermal, transmucosal (buccal, nasal, sublingual), epidural	Epidural, sublingual		
Time to onset (min)	1.5	1	0.75	<1
Time to peak effect (min)	4.5–8	2.5–5	1.5	1.5
Duration of peak effect (min)	20–30	30	15	
Duration of analgesic effect (min)	60–120	100–150	30–60	5–10
Analgesic plasma concentration (ng/mL)	0.6–3.0	0.5–2.5	50–300	0.3–3
Plasma concentration associated with loss of consciousness (ng/mL)	>20.0	>2.5	>400	>4
$t_{1/2a}$ (min)	1.7 ± 0.1	1.4 ± 0.3	1.31 ± 0.48	1
$t_{1/2b}$ (min)	13.4 ± 1.6	17.7 ± 2.6	9.4 ± 2.7	6
$t_{1/2c}$ (min)	*219 ± 10 (120–240)*	164 ± 22 *(120–180)*	*93.7 ± 8.3 (60–120)*	10–20 *(6–14)*
Vd_C (L/kg)	0.36 ± 0.07	0.16 ± 0.02	0.12 ± 0.04	0.1
$V_{d_{ss}}$ (L/kg)	4.0 ± 0.4 *(3–5)*	1.7 ± 0.2 *(2.5–3.0)*	1.0 ± 0.3 *(0.4–1.0)*	0.35 *(0.2–0.4)*
CL (mL/min/kg)	13 ± 2 *(10–20)*	12.7 ± 0.8 *(10–15)*	7.6 ± 2.4 *(3–9)*	40 *(30–60)*
Protein binding (%)	80–84	91–92.5	88.7–92.1	70
pKa	8.4	8.0	6.5	7.1
Non-ionized fraction at pH 7.40 (%)	8.5	20	89	67
Metabolism	CYP3A	CYP3A	CYP3A	Plasma and tissue esterases
Lipid solubility (octanol/water distribution coefficient)	813–816	1,727–1,778	128	18

Italic numbers indicate information from the Summary of Product Characteristics.

CL = clearance; CYP = cytochrome P450; IV = intravenous; $t_{1/2a}$ = distribution half-life; $t_{1/2b}$ = redistribution half-life; $t_{1/2c}$ = terminal elimination half-life; Vd_C = volume of distribution of the central compartment; $V_{d_{ss}}$ = volume of distribution at steady state.

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