Subcutaneous Drug Administration in Adults

Introduction

In palliative care, subcutaneous (SC) administration has traditionally been used extensively to administer analgesics, corticosteroids, antipsychotics, antiemetics, benzodiazepines, antibiotics, fluids, and other agents. The SC route, for both bolus administration and continuous infusion, is the preferred route when the oral route is unavailable.

The main indications for using the SC route are the inability to take medication by mouth because of dysphagia caused by a tumor of the mouth, pharynx, or esophagus, or by neurological disorders, as well as nausea and vomiting or malabsorption.

SC administration offers several advantages over the intravenous (IV) route. It is less invasive, and its ease of use reduces the need for frequent involvement of healthcare professionals, thereby lowering healthcare costs. However, when patients already have an IV catheter, it can be used in several circumstances. The SC route is also generally preferable to the intramuscular (IM) route because IM administration is more painful and requires repeated injections; these can be avoided with the SC route by inserting a butterfly-type or other small-gauge catheter. The SC route is also more suitable for self-administration than either the IV or IM route.

Continuous subcutaneous infusion (CSCI) is a widely used method in palliative care. It allows multiple symptoms to be controlled by combining compatible medications.

Diluents that may be used for CSCI include Sterile Water for Injection, 0.9% sodium chloride (NaCl), or 5% dextrose. Sterile Water for Injection is compatible with all medications used in palliative care, but because it is hypotonic, it may cause pain. The advantage of 0.9% sodium chloride is that it is isotonic and therefore is expected to cause fewer reactions at the infusion site. However, it is incompatible with cyclizine and diamorphine, and with haloperidol at concentrations greater than 1 mg/mL. 5% dextrose may also be used, except with alkaline drugs such as ketorolac, dexamethasone, phenobarbital, and furosemide, because it is acidic.

It is important to emphasize that, in many cases, the information provided here comes only from case reports.

Drug stability and compatibility may be affected by several factors, such as the drug salt, diluent, temperature, and infusion duration. Therefore, infusions should be checked regularly at short intervals (every 4 hours may be appropriate). Accordingly, the compatibility information presented here should be verified, and any change in color or cloudiness in the mixture after it has been mixed thoroughly should lead to its rejection.

Medications for Subcutaneous Administration

Opioids				
Medication	**Indications**	**Compatibility for continuous infusion**	**Dose**	**Notes**
Alfentanil [2]	Moderate to severe pain and dyspnea in patients with renal impairment	Haloperidol, hyoscine butylbromide, midazolam, ondansetron, levomepromazine, metoclopramide, octreotide	Dose equivalence: morphine 10 mg = alfentanil 1 mg Administer by continuous infusion	Generally used as a second-line opioid.
Fentanyl [1]	Moderate to severe pain and dyspnea in patients with renal or hepatic impairment	Ketamine, midazolam, ondansetron, haloperidol, hyoscine butylbromide, and metoclopramide	Dose equivalence: morphine 100 mg = fentanyl 1 mg Administer by continuous infusion	Generally used as a second-line opioid. In renal impairment, prefer alfentanil.
Morphine [2]	Moderate to severe pain and dyspnea	Hyoscine butylbromide, ketamine, haloperidol, levomepromazine, metoclopramide, midazolam, octreotide, ondansetron, ranitidine	Initial: 2.5 mg every 4 hours or 10–20 mg/24 hours Maximum: no maximum dose	Generally used as a first-line opioid.
Sufentanil [3]	Moderate to severe pain and dyspnea when fluid volume is limited	Hyoscine butylbromide, ketamine, clonazepam, haloperidol, levomepromazine, metoclopramide, midazolam, octreotide	Dose equivalence: morphine 1,000 mg = sufentanil 1 mg Administer by continuous infusion	Generally used as a second- or third-line agent. Its high potency allows administration in a small volume. Useful in renal impairment.
Other analgesics				
Ketorolac [6,7]	Mild to moderate pain; bone pain	Do not mix with other drugs. Dilute in the largest possible volume of NaCl.	Bolus: 30 mg 3 times/day CSCI: 30–90 mg/day; occasionally 120 mg/day	Prefer CSCI. If possible, limit use to 5 days; prolonged use has been reported.
Acetaminophen (paracetamol) [8]	Mild to moderate pain and fever	Not administered mixed with other drugs, but administered at the same site as several other drugs	1,000 mg/injection; in patients weighing less than 50 kg, 500 mg/injection	
Parecoxib [4,5]	Mild to moderate pain; bone pain	Do not mix with other drugs.	Initial: 40 mg once daily Maximum: 40 mg twice daily Continuous infusion: 40–80 mg in a total volume of 22 mL with NaCl	Because of its long half-life, continuous infusion is not necessary.
Adjuvants				
Ketamine [9]	Various types of pain, especially neuropathic pain	Alfentanil, clonazepam, haloperidol, levomepromazine, metoclopramide, midazolam, and morphine	Bolus: — CSCI: 1–2.5 mg/kg/24 hours; increase by 30–50%/day if needed, up to 500 mg/24 hours (maximum reported dose: 3.6 g/24 hours)	Because of its psychotomimetic effects, premedicate with haloperidol, lorazepam, or midazolam.
Benzodiazepines				
Clonazepam [10]	Seizures; sedation	Hyoscine butylbromide, ketamine, haloperidol,	0.5 mg every 2 hours; recommended maximum	For continuous infusion, do not use PVC

		levomepromazine, metoclopramide, midazolam, morphine	3 mg/24 hours; doses up to 8 mg/24 hours have been used. SC dose = oral dose	extension tubing because PVC may adsorb up to 50% of clonazepam. For bolus administration, dilute the 1 mg/mL ampule in 1 mL of Sterile Water for Injection.
Midazolam [2,13]	Anxiety, agitation, epilepsy, sedation	Alfentanil, hyoscine butylbromide, ketamine, haloperidol, fentanyl, levomepromazine, metoclopramide, morphine, octreotide, ondansetron	Bolus: 1–10 mg CSCI: 10–60 mg/24 hours	Much higher doses have been used.
Antipsychotics				
Haloperidol [2,11]	Delirium, agitation, nausea, and vomiting	Morphine. In 5% dextrose: with hyoscine butylbromide, ketamine, midazolam, and tramadol.	Dose depends on indication: 1 mg, repeat every 1–2 hours, up to 15 mg/day for agitation.	At concentrations greater than 1 mg/mL, it may precipitate in 0.9% NaCl.
Levomepromazine [2,12]	Delirium, agitation, sedation, nausea, and vomiting	Alfentanil, hyoscine butylbromide, ketamine, clonazepam, fentanyl, metoclopramide, midazolam, morphine, octreotide, ondansetron, ranitidine, sufentanil	6.25 mg once daily at bedtime Up to 300 mg/24 hours for sedation; higher doses have also been used	At higher doses, administer by CSCI. Because of its long half-life, lower doses may be administered as a bolus once or twice daily.
Antiepileptic drugs				
Valproic acid [14]	Epilepsy, delirium, bipolar disorder	No compatibility studies are available. Do not mix with any other drug.	CSCI: 600–1,200 mg/24 hours	Oral dose:SC dose = 1:1.
Phenobarbital [17]	Epilepsy; sedation	Do not mix with any other drug.	Bolus: 200 mg, rotating sites CSCI: up to 3,600 mg/24 hours	For doses ≤1,600 mg, dilute in 17 mL of Sterile Water for Injection. For doses >1,600 mg, dilute in NaCl.
Levetiracetam [15,16]	Epilepsy	Hyoscine butylbromide, clonidine, haloperidol, metamizole, metoclopramide, midazolam, morphine	Bolus: in 100 mL every 12 hours over approximately 30 minutes CSCI: dose equal to the oral or IV dose	Oral dose:SC dose = 1:1.
Antibiotics				
Ampicillin [32]	Infections	Do not mix with other drugs.	1 g in 50 mL of 0.9% NaCl, infused over 20 minutes.	
Cefepime [32]	Infections	Do not mix with other drugs.	1 g in 50 mL of 5% dextrose, over 30 minutes.	May cause mild local adverse effects, such as pain, swelling, and erythema.
Ceftriaxone [18]	Infections	Do not mix with other drugs.	Bolus: in 3.5 mL Infusion: in 20 mL over 15–30 minutes	Only one case of severe SC necrosis has been reported, with slow recovery.
Ertapenem [20]	Infections	Do not mix with other drugs.	Bolus: 1 g diluted in 3 mL of lidocaine, over 1 minute	A case of skin necrosis occurred with bolus

			(once daily) CSCI: 1 g in 50 mL of 0.9% NaCl over 30 minutes (once daily)	administration, with rapid improvement following local care.
Meropenem [37]	Infections	Do not mix with other drugs.	1 g diluted in 50 mL of 0.9% NaCl, infused by gravity over 30 minutes, followed by a final infusion of 10–20 mL of NaCl over 10 minutes.	
Benzathine penicillin G [33–35]	Infections; syphilis; prevention of rheumatic fever	Do not mix with other drugs.	Inject over 2–3 minutes, or co-administer with 1% lidocaine (up to 5 mL) over 8–20 minutes (mean: 14 minutes).	10.8 million IU every 13 weeks produced an effect similar to 1.2 million IU every 4 weeks for prevention of rheumatic fever.
Piperacillin/tazobactam [19]	Infections	Do not mix with other drugs.	CSCI: 4.5 g in 50 mL of 0.9% NaCl, infused over 6 hours, 4 times daily.	At the end of the 6-hour infusion, the site was massaged and the next dose was started. The infusion was administered in the thigh, with the site switched to the other thigh after 24 hours.
Temocillin [36]	Infections caused by ESBL- and AmpC-producing microorganisms	Do not mix with other drugs.	2 g diluted in equal parts Sterile Water for Injection and 1% lidocaine, to a total volume of 4.3 mL, administered by infusion pump over 20 minutes.	
Tobramycin [32]	Infections	Do not mix with other drugs.	80 mg in 50 mL of 0.9% NaCl over 20 minutes.	
Other medications				
Hyoscine butylbromide [2,21]	Smooth muscle spasms, drying of secretions, bowel obstruction	Alfentanil, fentanyl, haloperidol, levomepromazine, midazolam, morphine, octreotide	Bolus: 20 mg every 6–8 hours CSCI: 60–120 mg/24 hours	Higher doses have been used, up to 240 mg/24 hours [23].
Dexamethasone [29]	Multiple uses in palliative care	Generally, do not mix with other drugs.	Bolus: up to 8 mg every 8–12 hours CSCI: possible, but not necessary	May be administered once daily, but volume is a limiting factor. Do not administer more than 2 mL at the same site.
Furosemide [24,25]	Edema, dyspnea	Do not mix with other drugs.	Bolus: up to 160 mg twice daily CSCI: 40–300 mg/24 hours	The injectable furosemide concentration is 10 mg/mL, so large bolus doses may be problematic. Do not mix with 5% dextrose.
Metoclopramide [2,28]	Nausea and vomiting	Alfentanil, fentanyl, levomepromazine, midazolam, morphine, octreotide, ondansetron	Bolus: 10 mg up to 3–4 times/day CSCI: 30–120 mg/24 hours	

Octreotide [2,30]	Bowel obstruction, refractory diarrhea, carcinoid tumors, and others	Alfentanil, hyoscine butylbromide, haloperidol, levomepromazine, metoclopramide, midazolam, morphine, ondansetron	Bolus: 50–200 mcg every 8 hours CSCI: 150–1,500 mcg/24 hours	Bolus injection may be painful; this can be minimized by warming the ampule to body temperature.
Omeprazole [23]	Gastrointestinal bleeding, gastroesophageal reflux, dyspepsia	Do not mix with other drugs.	40 mg in 100 mL, infused over 3–4 hours/day.	
Esomeprazole [22]	Gastrointestinal bleeding, gastroesophageal reflux, dyspepsia	Do not mix with other drugs.	40 mg in 50 mL, infused over 1 hour/day.	
Pantoprazole [31]	Gastrointestinal bleeding, gastroesophageal reflux, dyspepsia	Do not mix with other drugs.	40 mg IV powder for injection, reconstituted in 10 mL of 0.9% NaCl; administer as a bolus over approximately 2 minutes daily, rotating sites.	
Ondansetron [2,26,27]	Nausea and vomiting, opioid-induced pruritus, diarrhea associated with carcinoid syndrome	Alfentanil, hyoscine butylbromide, fentanyl, haloperidol, levomepromazine, metoclopramide, midazolam, morphine, octreotide	Bolus: 4–8 mg, up to 3 times/day CSCI: up to 24 mg/24 hours	

Unless otherwise specified in the table, 0.9% NaCl should be considered the diluent. Unless another instruction is specified in the table, for CSCI the diluent volume should be sufficient to fill the syringe to the intended volume. If CSCI includes more than one drug, combine the drugs before adding the diluent.
For bolus administration, a diluent may not be necessary unless otherwise specified in the table.
The doses listed refer to patients without renal or hepatic impairment; if either is present, the dose may need to be adjusted accordingly.
Infusion recommendations are limited to 24 hours because of the physical, chemical, and microbiological stability of the solutions. However, infusions lasting several days have been used.

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