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BACKGROUND

Over the last decade, administration of medications like morphine, hydromorphone, metoclopramide, haloperidol or midazolam by subcutaneous route has regain popularity in palliative care and geriatric setting.^{1,2} Similarly, subcutaneous rehydration also called hypodermoclysis seems to be a good alternative to intravenous rehydration in elderly patients and terminal cancer patients when oral intake is severely restricted.^{3,4} However, the majority of drugs used are unlicensed for subcutaneous use and there is a lack of information in the literature about this practice.

OBJECTIVES

- Survey of subcutaneous (SC) drug use and hypodermoclysis in a geriatric hospital department (404 beds, mean age of patients 85)
- Evaluation of license status and systematic literature review of 34 drugs used subcutaneously in geriatric setting and comparison with practice

DESIGN

- Standardized questionnaire to 27 nursing teams and 52 physicians
- License status in official on-line information for Switzerland (CH), France (F), Germany (D) and United Kingdom (UK) (Compendium suisse des médicaments, Vidal, Rote Liste, BNF in March 2003)
- Systematic literature review using Medline (1966 – March 2003) and Embase Geriatrics & Gerontology (1992 – 2002) of articles published in French, German or English and quality evaluation⁵

RESULTS

Evaluation of practices - general datas:

- Response rate: 22 (81%) nursing teams and 37 (71%) physicians (n = 59)
- Use of SC route: palliative care (83% of questionnaire), dehydrated patients (54%), patients with central nervous disorders (25%) or with cancer (22%), and when oral or IV administration is impossible (73% resp. 68%) or because of comfort for the patient (27%)
- Adverse reactions: see Fig. 2

Evaluation of practices – administration of drugs:

- Frequency: SC route is daily used in the department
- Drugs mainly used: morphine (98%), haloperidol (90%), furosemide (70%), hydromorphone (56%) (Fig.1)
- Site of injection: thighs (100%), arm (82%), abdominal wall (77%)
- Mode of administration: slow (82%), bolus injection (36%), syringe driver (9%)

Evaluation of practices – administration of fluids:

- Frequency: Hypodermoclysis is used many times / week
- Fluids mainly used: NaCl 0.9% (95%) and Glucosalin (30%) (Fig.1)
- Site of injection: thighs (96%), back (23%), arm (18%)
- Mode of administration: mean duration 7 days (min 1, max 21); 250 ml to 1000 ml / inj. site in 2 to 24 hours and 500 ml to 2000 ml/patient/day

Fig. 1

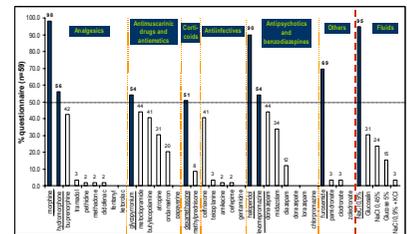
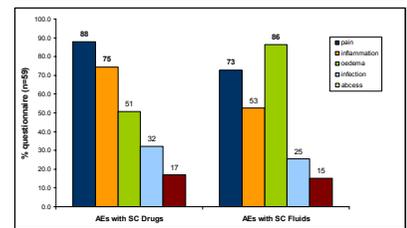


Fig. 2



Evaluation of license status:

- Only 13 of 34 drugs (38%) licensed for SC use in CH (8), UK (7), F (6) or D (6) (Tab.1)

Systematic literature review:

- Of 231 published articles, 43 identified as interesting for SC drug use and 25 for rehydration
- Only morphine and rehydration intensively evaluated in the literature in studies of high level of evidence (Tab.2)
- Fentanyl, hydromorphone, pethidine, butylscopolamine, ceftriaxone, and chlormpromazine at least evaluated in one study of good methodology (Tab.2)
- Haloperidol and furosemide, although frequently used, are unlicensed in all four countries and there is no robust studies in the literature

Tab. 2

Article	Country	Type of study	n patients	Age and type of patients	Subject	Commentary
Miyakoshi et al. 2002	France	Randomised double-blind controlled trial	58	MF: 42-77 yr, terminal ill	Butylscopolamine + chlorpromazine SC vs intravenous SC	Chlorpromazine + chlorpromazine better in management of nausea and anxiety, but not pain
Mohr-Cosca et al. 2000	France	Randomised open controlled trial	25	MF: mean 82 yr, respiratory failure	Ceftriaxone SC vs IV	SC route equivalent with IV route, good tolerance
Hunter et al. 1999	Australia	Randomised double-blind cross-over controlled trial	23	MF: 48-89 yr, mean 78.5 yr, advanced cancer	Fentanyl vs Morphine SC	No significant differences between both drugs
Wills PF	USA	Randomised double-blind controlled trial	120	MF: mean 53 yr, surgical (orthopedic, urologic and gynecological)	Hydromorphone SC PCA vs IV PCA vs morphine SC PCA vs IV PCA	SC PCA acceptable alternative to IV PCA
Brava et al. 1995	Canada	Randomised double-blind two-way cross-over pharmacokinetic trial	9	MF: mean 88 yr, cancer pain	Morphine oral (controlled release) vs SC	Oral vs SC absorption comparable at 3.5 h dose ratio
Copetti et al. 1997	Colombia	Randomised double-blind controlled trial	112	MF: 14-85 yr, acute encephalopathy	Morphine 4 vs intravenous R vs morphine SC	Morphine 4 vs SC effective in hypotensive R
Crocker et al. 1997	Australia	Randomised double-blind cross-over trial	39	MF: 50-78 yr, mean 50 yr	Morphine 4 vs SC	Morphine SC effective as IV
Capron et al. 1995	Canada	Prospective, cohort study	63	MF: mean 58, advanced cancer	Morphine SC vs cyclophosphamide SC, hydromorphone SC vs cyclophosphamide SC	Morphine vs cyclophosphamide equivalent; 8/21 desatrated cyclophosphamide SC
McLure et al. 1991	France	Randomised, double-blind controlled trial	153	MF: 57 yr, advanced surgery for cancer	Morphine SC vs hydromorphone EPi vs morphine EPi	Analgesic better with EPi response but more specific, better tolerance
Klein et al. 1996	France	Randomised double-blind cross-over controlled trial	10	MF: 22-35 yr, mean 53, cardiovascular cancer	Morphine EPi vs CSCD	Morphine EPi vs CSCD comparable in effectiveness and acceptability
Kelly et al. 2003	France	Randomised controlled trial	41	MF: 70-81 yr, late hip replacement	Morphine IV PCA vs SC	Pain score lower with IV PCA, side-effect similar
Lafitte et al. 1992	France	Randomised controlled trial	20	MF: 72 yr, cyclophosphamide	Morphine PERI vs SC	Post-operative respiratory function better with PERI morphine
Murphy et al. 1992	USA	Randomised controlled trial	30	MF: mean 60 yr, cardiac surgery	Morphine IV PCA vs NSA SC	Alternative to NSA
Neves et al. 1997	USA	Prospective, within patient one-way cross-over trial	43	MF: 38-83 yr, med 67, chronic cancer pain	Morphine CIV vs CSCD	Morphine CIV vs CSCD equivalent
Rowell et al. 1997	UK	Randomised, pharmacokinetic controlled trial	40	MF: mean 77 yr, advanced or orthopedic surgery	Morphine SC vs IV	Time to effect of oral analgesic longer than IV SC at defined doses
Vermorel et al. 1998	Belgium	Prospective pharmacokinetic trial	34	MF: 50-81 yr, cancer pain	Pharmacokinetics of Morphine CSCD	Large inter- and interindividual variability of morphine disposition
Shaw et al. 1995	UK	Randomised controlled trial	44	SV: orthopedic surgery	Pethidine intravenous vs SC	Intravenous route superior to SC route in analgesia
Chalmers et al. 1994	UK	Randomised controlled trial	34	MF: 60-81 yr, acute stroke	Hypodermoclysis with NaCl/0.9% SC vs IV hydration	SC effective alternative to IV
Compton et al. 2003	Canada	Prospective cohort study	55	MF: 53-100 yr, mean 82.7, frail older	Hypodermoclysis SC vs IV hydration	Hypodermoclysis effective and safer than IV, fewer reactions at SC
Loyche et al. 1999	New Zealand	Cross-over pharmacokinetic trial	6	MF: 70-91 yr, healthy	Absorption of NaCl 0.9% SC vs IV	SC infusion of NaCl 0.9% equivalent to IV
Chiu et al. 1994	France	Randomised controlled trial	60	MF: mean 82 yr, cognitive impairment	Hypodermoclysis SC vs IV hydration	SC fluid therapy is treatment of choice for constipated elderly
Reisman et al. 1997	Canada	Systematic Review	660	Randomised elderly patients	Hypodermoclysis vs oral electrolyte-containing fluids	Hypodermoclysis safe with low fluid-containing fluids
Sinek et al. 2003	Germany	Randomised open controlled trial	96	MF: mean 83.3 yr, mild to moderate dehydrated	Hypodermoclysis with NaCl/0.9% SC vs IV hydration	Both techniques comparably safe and effective

Tab. 1

Drug Class	Analgesics					Antimuscarinic drugs		Corticoid	Anti-infectives	Antipsychotics
	opioid	hydromorphone	buprenorphine	tramadol	pethidine	butylscopolamine	atropine			
CH	x	x	x	x	x	x	x	x		
UK	x				x	x	x	x		x
F	x	x				x	x		x	x
D	x	x		x		x	x			

CONCLUSIONS

SC drug use and hypodermoclysis is performed daily in our geriatric department. Only few drugs are licensed for SC route and well evaluated in the literature. Consequently physicians strongly engaged their responsibility in the prescription. More datas of good quality are necessary to validate the use of haloperidol and furosemide by SC route.

REFERENCES

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