

Hypodermoclysis: a literature review to assist in clinical practice

Hipodermóclise: revisão de literatura para auxiliar a prática clínica

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ABSTRACT

The aim of this study was to analyze the information available in the literature about the drugs that can be administered through hypodermoclysis and the resulting impact that this information may have on the routine of the pharmacist working at a hospital. The study was based on a review of the literature. The results showed positive points of the procedure, but little specific information about medications such as routes of administration, standard dilutions, optimal doses, etc. Thus, it was possible to verify that there is no definite information as to the correct way to administer the drugs in this route, even though this is an effective and safe option, according to the literature. The lack of information has a negative impact on the support provided by the pharmacist to the nursing staff to ensure that the drug actually reaches its therapeutic goals safely.

Keywords: Hypodermoclysis; Palliative care; Infusions, subcutaneous

RESUMO

O objetivo desse trabalho, foi analisar, na literatura, as informações disponíveis sobre os medicamentos que podem ser administrados através da hipodermóclise e o impacto que a informação pode acarretar na rotina do farmacêutico dentro de uma unidade hospitalar. O estudo foi baseado em uma revisão de literatura. Os resultados encontrados, demonstraram pontos positivos do procedimento, porém foram localizadas poucas informações específicas sobre medicamentos, como métodos de administração, padrões de diluição, dose ideal etc. Dessa forma, foi possível verificar que não há informações definitivas quanto ao modo mais correto de se administrar as drogas por essa via, mesmo sendo esta uma opção eficaz e segura, conforme a literatura. A falta de informação impacta negativamente no suporte

realizado pelo farmacêutico à equipe de enfermagem para garantir que o medicamento realmente alcance seus objetivos terapêuticos com segurança.

Descritores: Hipodermóclise; Cuidados paliativos; Infusões subcutâneas

INTRODUCTION

Hypodermoclysis is also known as the administration of fluids by the subcutaneous route. It is an ancient practice and was first reported in 1913, but because of the adverse events resulting from its inadequate use, such as the use of hypertonic solutions, the practice was abandoned.⁽¹⁻⁴⁾

It has been used in patients who present with diagnoses of moderate dehydration caused by severe dysphagia, dementia, intestinal obstruction due to neoplasms, and somnolence. There is also the possibility of administering medications to those patients who have no conditions for a peripheral venous access puncture.^(1,2,4-9)

Hypodermoclysis is also described as a simple practice and less expensive than the other techniques.⁽¹⁰⁾

The medications and fluids given by hypodermoclysis are absorbed by means of capillary diffusion mechanisms. Patient edema and hematomas may hinder treatment.^(11,12) The pharmacokinetics are similar to those of medications administered by intramuscular route, but display a prolonged time of action, besides better tolerability for

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those medications with a pH close to neutral and that are hydrosoluble.⁽¹¹⁾

In order to facilitate administration of medications by hypodermoclysis, some literature suggests the use of hyaluronidase, as this is an enzyme that decomposes the hyaluronic acid present in the tissue, leading to decreased viscosity and thus increasing the rate of absorption of the drugs given.⁽³⁾

There are locations (puncture sites) that are more appropriate for therapy, such as the deltoid region, anterior chest region, scapular region, abdominal regional, and anterior and lateral sides of the thighs. (Figure 1)

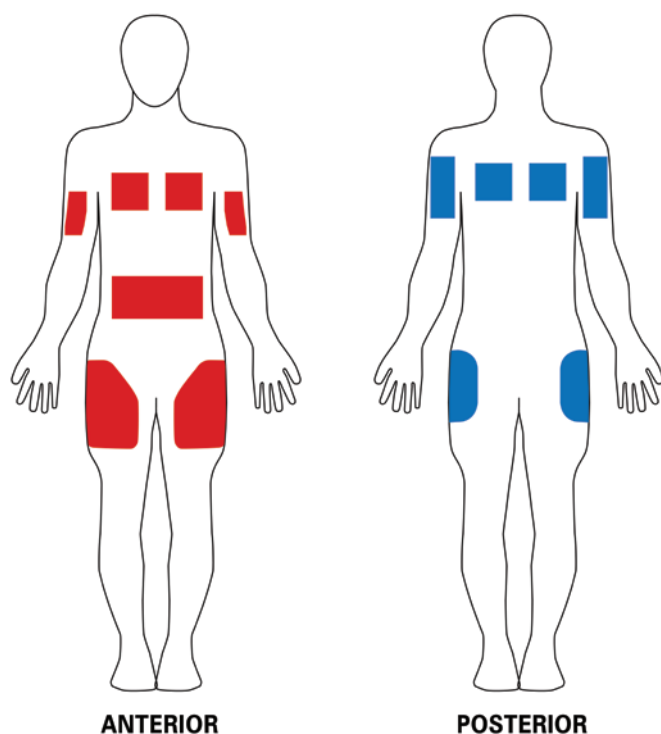


Figure 1. Puncture sites

In Brazil, this technique has been gaining acceptance for use in patients in Palliative Care or in those who are very old or debilitated.

Subcutaneous therapy does not cover only replacement fluids, but also medications that have been prescribed through this route, such as antimicrobials and analgesics, among others.

Some of these medications have no description on the packet insert as to the possibility of being given by this technique; therefore, when prescribed, we consider their use as “off-label”.

For professional prescribers, in general, indication of route of administration is based on the international literature or on one’s own clinical experience, which is not reported in official articles.

For the local Pharmacy, the lack of reliable information generates certain difficulties when evaluating a medical prescription, as well as in instructing the nursing team as to the necessary care for use of the prescribed drug, since each medication has its own exclusive characteristics, such as pH, stability, besides appropriate dilution and diluent volumes.

Since there is little information in literature on this topic, the interest arose to analyze, by means of this study, what national and international literature has become available on hypodermoclysis and to what extent this information may be valuable to the pharmacist, since this professional is the one responsible for the medications within a hospital.

METHODS

This is a bibliographic research, with review of literature. Books and manuals on Palliative Care were consulted, and searches conducted for articles and guidelines in the databases Scientific Electronic Library Online (SciELO), MEDLINE, and Google Scholar. The keywords used were “hypodermoclysis”, “Palliative Care”, and “subcutaneous route”, published in Portuguese and English, within a timeframe that included the years 1999 to 2012.

The articles were analyzed according to the objective proposed so that the papers that had information related to the use of medications and the method of their use, hydrating solutions (0.9% sodium chloride, 0.45% sodium chloride, and 5% glucose), besides the advantages and disadvantages of the technique and possible adverse reactions.

Many of the studies and guidelines found in preparing this study were international. Even so, they do not offer a large amount of information as to the topic, especially as to the use of drugs.

The information was tabulated on an electronic spreadsheet (EXCEL) and presented in the form of charts and tables.

To prepare the chart related to compatibilities, the Micromedex® electronic database was used as a tool.

Chart 1 presents information on the medications cited in the articles.

Chart 1. Table of medications most often used by subcutaneous route

Drug	Indication	Doses	Most indicated diluent	Infusion time indicated	Comments
Ampicillin ^(#)	Infections	500mg/day	*	*	*
Atropine	*	1.2mg/once a day	*	*	*
Cefepime ^(#)	Infections	1g/day	SS	*	*
Cefotaxime ^(#)	Infections	500mg/day	SS	30 minutes	*
Ceftazidime ^(#)	Infections	500mg/day	SS	30 minutes	*
Ceftriaxone ^(#)	Infections	1g/day	SS	30 minutes	*
Ketorolac	Intense pain	30-90mg/day	SS	*	Exclusive route
Cyclizine	Nausea and vomiting	25-50mg every 8 hours (maximum of 150mg/day)	Continuous inf.=DW	*	Incompatible with SS
Clonazepam	Agitation and anxiety	5-8mg/day	SS or DW	*	Is an irritant, dilute to maximum tolerated
Dexamethasone	1. Increased intracranial pressure 2. Reduction of peritumor edema 3. Dyspnea 4. Nausea and vomiting	1. 4-16mg/day 2. 4-40mg/day 3. 8-24mg/day 4. 8-20mg/day	SS or DW	*	Exclusive route
Diclofenac	Pain	75-150mg/day	SS	*	Is an irritant, dilute to maximum tolerated
Dipyrrone	Pain	1g up to every 6 hours	SS	*	Exclusive route
Scopolamine	Intestinal cramps	60-180mg/day Maximum of 40mg/day in continuous infusion	DW	*	*
Famotidine	Gastric protector	*	*	*	*
Phenobarbital	Confusion	200mg/day	DW	*	Exclusive route, even though compatible with morphine
Fentanyl	Pain	Usual: 100 -1,000mcg/day Rescue 10mcg every hour	SS	1mL/h=5mcg/h (solution of 500mcg in 100mL of diluent)	*
Furosemide	Dyspnea due to pulmonary congestion	20-40mg	SS	*	*
Granisetron	Nausea and vomiting	3-9mg/day	50mL SS	> 10 minutes	*
Haloperidol	Nausea and vomiting Sedation, agitation	2.5-10mg/day	DW	*	Maximal concentration of 2mg/mL. SS may precipitate
Hydromorphone	Pain	50% of oral dose	*	*	*
Hydroxyzine	Antiallergic	*	*	*	*
Levomepromazine	Intense nausea and vomiting	5-100mg/day Maximum dose of 200mg	SS	*	Is an irritant, dilute to maximum tolerated
Methadone	Intense pain	50% of oral dose	SS	60mL/h	Is an irritant, vary the puncture site every 24 hours
Metoclopramide	Nausea and vomiting	30-120mg/day	DW	*	Is an irritant, dilute to the maximum tolerated
Midazolam	1. Agitation and confusion in terminal patients 2. Multifocal myoclonus 3. Hiccups 4. Sedation	1. 10-60mg/day 2. 10-30mg/day 3. 30-120mg/day 4. Initiate with 1mg/h and increase to 4mg/h	SS or DW	*	Is an irritant, dilute to the maximum tolerated
Morphine	Pain and dyspnea	50% of oral dose	SS or DW	*	A dose of 10mg/mL can be given every 4 hours
Naproxen	Pain	550-600mg/day	*	*	Incompatible with morphine
Octreotide	1. Reduced gastric secretion, motility, vomiting and diarrhea 2. Intestinal obstruction 3. Intractable diarrhea	1. 300- 600mcg/day (maximum of 1,500mcg) 2. 250-500mcg (maximum of 750mcg) 3. 50-500mcg (maximum of 1,500mcg)	SS	*	Is an irritant
Ondansetron	Nausea and vomiting	8-24mg/day	SS or DW	*	*
Promethazine ^(#)	Nausea, Antiallergic	12-25mg/day	*	*	*
Ranitidine	Gastric protector	50-150mg/day (maximum of 300mg)	DW	*	*
Tobramycin ^(#)	Infections	75mg/day	*	*	*
Tramadol	Pain	100-600mg/day	SS	*	*

Adapted from: Ferreira KA and Santos AC.⁽⁷⁾^(#) Pereira I. Cuidado paliativo. São Paulo: CREMESP, 2008. Hipodermóclise, p. 260-72. DW: distilled water; SS: saline solution; *: no information available.

RESULTS

According to the methodology cited for search of information, 17 pieces of literature (Chart 2) and an electronic database were selected.

The selection of articles resulted in the following findings: five papers covering only information related to the procedure of hydration, *i.e.*, no medications were mentioned, four only focused on the use of medications, and eight presented both types of information. Only five articles cited information related to the form of preparation and administration of the medications.

Of the articles selected, 10 had information related to the advantages and disadvantages of the method, (Chart 3), and only two references did not cite any adverse reactions.^(5,13)

Most often reported adverse reactions were pain, inflammation at the puncture site, and even edema and tissue necrosis.^(3,6,8,12,14,15)

In one of the articles located, 57 patients were accompanied at a Prolonged Stay Institution for the Elderly (ILPI, acronym in Portuguese) and received hydration by hypodermoclysis; 88% of them showed improvement of the general clinical status and 84% showed improvement in cognitive status after the use of hypodermoclysis.⁽¹²⁾

As to information related to medications, very little has been written since few drugs have been studied to date using this route, and few have license for use in subcutaneous infusions.⁽¹⁴⁾ According to one of the articles analyzed, in which an open questionnaire was answered by physicians as to the types of medications most commonly

Chart 2. Literature selected in databases

Author	Title	Year	Medications/hydration/both/not cited	Advantages and disadvantages	Adverse reactions	Mode of preparation and administration of medications
Pereira I ⁽¹⁾	<i>Cuidado Paliativo. Conselho Regional de Medicina do Estado de São Paulo - CREMESP. Hipodermoclise</i>	2008	Both	Yes	Yes	No
Jain S et al. ⁽²⁾	Subcutaneous fluid administration – better than the intravenous approach?	1999	Both	Yes	Yes	No
Conselho Regional de Enfermagem de São Paulo ⁽³⁾	<i>Hipodermoclise</i>	2009	Both	Yes	Yes	No
Takaki CY et al. ⁽⁴⁾	<i>Hipodermoclise: o conhecimento do enfermeiro em unidade de internação</i>	2010	Both	Yes	Yes	No
Marques C et al. ⁽⁵⁾	<i>Terapêutica subcutânea em cuidados paliativos</i>	2005	Medications	No	No	No
Yap LK et al. ⁽⁶⁾	Hypodermoclysis or subcutaneous infusion revisited	2001	Hydration	No	Yes	No
Ferreira KA et al. ⁽⁷⁾	Hypodermoclysis and administration of medications by subcutaneous route: A technique from the past with a future	2009	Both	No	Yes	Yes
Griffiths A ⁽⁸⁾	Clinical Guideline for Subcutaneous Infusion (Hypodermoclysis). INHS South Gloucestershire	2010	Hydration	Yes	Yes	No
Remington R et al. ⁽⁹⁾	Hypodermoclysis to Treat Dehydration: A Review of the Evidence	2007	Hydration	Yes	Yes	No
Sasson M et al. ⁽¹⁰⁾	Hypodermoclysis: an alternative infusion technique	2001	Hydration	Yes	Yes	No
Instituto Nacional do Câncer ⁽¹¹⁾	<i>Série Cuidados Paliativos. Terapia Subcutânea no Câncer Avançado</i>	2009	Both	Yes	Yes	Yes
Arinzon Z, et al. ⁽¹²⁾	Hypodermoclysis (subcutaneous infusion) - effective mode of treatment of dehydration in long-term care patients	2004	Hydration	No	Yes	No
Frasca D, et al. ⁽¹³⁾	Pharmacokinetics of Ertapenem Following Intravenous and Subcutaneous Infusions in Patients	2010	Medications	No	No	Yes
NHS Greater Glasgow and Clyde ⁽¹⁴⁾	Guideline for the Use of Subcutaneous Medications in Palliative* Care for Adults	2010	Medications	Yes	Yes	No
Azevedo EF, et al. ⁽¹⁵⁾	Administration of antibiotics subcutaneously: an integrative literature review	2012	Medications	No	Yes	No
Azevedo EF, et al. ⁽¹⁶⁾	<i>Manual de Cuidados Paliativos. Academia Nacional de Cuidados Paliativos – ANCP. Hipodermoclise: um método alternativo para infusão de fluidos e medicações pela via subcutânea</i>	2009	Both	Yes	Yes	Yes
Fonzo-Christe C, et al. ⁽¹⁷⁾	Subcutaneous administration of drugs in the elderly: survey of practice and systematic literature review	2005	Both	No	Yes	Yes

Most classes of medications already in use for this route are opioids, antibiotics, antiemetics, and sedatives. Chart 3 shows some information related exclusively to medications that have already been reported in literature regarding use of hypodermoclysis.

In addition to these drugs cited on the table, there are other papers that report the use of other antimicrobials, such as ertapenem, amikacin, gentamicin, and teicoplanin, but these articles still contain limited information and apparently demonstrate equivalence when compared to the usual routes, although the numbers of patients used were very small.⁽¹⁵⁾

A large part of the adverse reactions mentioned in the articles occurred due to inadequate use, such as for example, unsuitable puncture sites, medication inappropriate for that route of administration, inadequate dilution, and lack of rotation of puncture site (change every 96 hours).⁽¹¹⁾

By means of this research, we noted that the information related to the form of preparation and administration of medications is not yet standardized. Therefore, we must evaluate the patients' conditions before indicating the administration route, and if there are other drugs or even solutions that are already being administered by the subcutaneous route, such as a saline solution, for example. We should also remember that the limit of fluids for infusion over a period of 24 hours cannot surpass 3,000mL divided into two different puncture sites (1,500mL at each puncture every 24 hours).^(1,2,6,10) This issue may be minimized since one or more drugs may be given by a single infusion system.

Chart 4 presents information related to compatibility among a few medications.^(16,18)

DISCUSSION

By means of the results found, we observed that the hypodermoclysis technique is a safe, effective, low cost, and easily applicable methodology^(5,12) that seems to bring some benefits.^(1-4,8-11,14,16)

However, there are still few original studies available on this topic, especially those that include the administration of medications; the working samples located were small, making it difficult to reach a definition as to the efficacy in use of these medications, which also was made evident by a few authors in their studies.^(13,15) The original studies used to compose this project focused on issues related to hydration, especially in the elderly.^(2,6,9,10,12)

Of the medications already indicated and commonly prescribed for the subcutaneous route, as was reported in one of the studies, most are prescribed primarily

based on clinical practice more than on literature per se.⁽¹⁷⁾ Additionally, their form of administration ends up being in accordance with its intravenous use, since until now, the most appropriate form for preparation and administration to the patients has not yet been established; however, in literature, there is information that recommends a dilution of 1mL of medication to 1mL of diluent.⁽¹⁶⁾ Nevertheless, this information is still not a consensus for the use of all the drugs prescribed, as each one of them has their own profile regarding dilution, stability, pH, and these issues may be fundamental in order to avoid adverse events.

If the technique is not applied appropriately, it may cause problems for the patient as described in the results of this article. In this sense, instead of bringing the possible benefits by the technique, it causes more harm.

Of the 17 articles used, only one paper did not cover specific information as to the technique. This one sought to know what the level of knowledge is in a nursing team as to the technique, a fact that called our attention, since many nurses who answered the questionnaire (71%) were not familiar with the method.⁽⁴⁾ This reinforces the idea that due to scarce availability of information in literature, or availability of repeated information, the technique is not amply made known, and this profile of medical prescription caused great difficulty for the pharmacist and the accompanying team in giving quality orientation so that there is safe management of the techniques of preparation and administration of drugs using the subcutaneous route.

The chart drawn up on the compatibilities shows some possibilities of optimizing puncture sites, as well as volumes of administration, which are capable of providing greater comfort for the patient due to less patient manipulation.

The greatest difficulty in this study was locating information related to the method of preparation and the time of administration of the medications, as was cited in the results, in which only five described some form of preparation and administration of medications.^(7,11,13,16,17)

The pharmaceutical industry should, on the other hand, invest and prepare studies focused on this administration technique. This can become a distinguishing factor on the market, since such a technique is geared towards patients under Palliative Care and the elderly, as these patients, on the other hand, present with reduced muscle mass, difficulty in puncturing peripheral accesses, and difficulties in swallowing.

New studies could be prepared in a considerable portion of a specific population, in order to also construct

a safety profile for the patient and for the medication itself.

CONCLUSION

The complication of this information may direct the pharmacist, as well as the medical and nursing teams in evaluating the medications to be given by hypodermoclysis, in this way offering a guarantee of therapy success and patient safety, besides decreasing risks of adverse events related to administration by such a route.

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