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COMPLICATIONS OF HYPODERMOCLYSIS IN PATIENTS UNDER PALLIATIVE CARE: A SYSTEMATIC REVIEW

*Complicações da hipodermóclise em pacientes sob cuidados paliativos: uma revisão sistemática**Complicaciones de la hipodermocclisis en pacientes bajo cuidados paliativos: una revisión sistemática***Isabel Yovana Quispe Mendoza**¹ **Raquel Eustaquia de Souza**¹ **Clarissa de Jesus Ferracioli**² **Rafaela Pereira Rocha Reis**¹ **Carlos Roberto Gomes Junior**¹ **Giovana Paula Rezende Simino**¹ 

ABSTRACT

Objective: to identify evidence in the literature about local complications observed when using hypodermoclysis in patients under Palliative Care. **Method:** this was a systematic review to assess local and regional complications of the hypodermoclysis catheter insertion site in patients under Palliative Care. Searches were performed from November to December 2020 using the following databases: MEDLINE, PubMed, LILACS, BDENF and SciELO. A systematic review prism model was adopted. **Results:** the following evidence was identified: the most prevalent complications resulting from the use of hypodermoclysis were edema and erythema, with a predominance of needled catheter use, mainly in the abdominal and infraclavicular regions. Among the most administered solutions and medications, the following stood out: 0.9% NaCl, KCl and opioids. **Conclusion:** there is a need to intensify the development of research with improved design and methodological rigor, resulting in greater evidence regarding the investigated topic.

DESCRIPTORS: Nursing care; Hypodermoclysis; Subcutaneous Infusion; Injection site reaction.

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RESUMO

Objetivo: identificar evidências na literatura acerca das complicações locais do uso da hipodermóclise em pacientes sob Cuidados Paliativos. **Método:** trata-se de uma revisão sistemática para avaliar as complicações locais e regionais no sítio de inserção do cateter da hipodermóclise em pacientes sob Cuidados Paliativos. As buscas foram realizadas de novembro a dezembro de 2020 nas bases de dados: MEDLINE, PubMed, LILACS, BDNF e no SciELO. Foi adotado modelo prisma de revisão sistemática. **Resultados:** foram identificadas as seguintes evidências: as complicações mais prevalentes decorrentes da utilização da hipodermóclise foram edema e eritema, com predominância da utilização de cateter agulhado principalmente na região abdominal e infraclavicular. Dentre as soluções e medicamentos mais administrados destacam-se: o NaCl 0,9%, o KCl e os opioides. **Conclusão:** há a necessidade de intensificar o desenvolvimento de pesquisas com melhor delineamento e rigor metodológico, produzindo evidências fortes relativas ao tema investigado.

DESCRITORES: Cuidados de enfermagem; Hipodermóclise; Infusões Subcutâneas; Reação no local da injeção.

RESUMEN

Objetivo: identificar evidencias en la literatura sobre las complicaciones locales del uso de hipodermoclysis en pacientes en Cuidados Paliativos. **Método:** se trata de una revisión sistemática para evaluar las complicaciones locales y regionales del lugar de punción de la aguja de hipodermoclysis en pacientes en Cuidados Paliativos. La búsqueda fue realizada de Noviembre a Diciembre de 2020 en las bases de datos: MEDLINE, PubMed, LILACS, BDNF y SciELO. Fue adoptado el modelo prisma de revisión sistemática. **Resultados:** las complicaciones más prevalentes decorrentes de la utilización de la hipodermoclysis fueron edema y eritema, predominó el uso de aguja metálica "tipo mariposa", principalmente en la región abdominal e infraclavicular. Entre las soluciones y medicamentos más administrados fueron el NaCl 0,9%, o KCl y los opioides. **Conclusión:** existe la necesidad de intensificar el desenvolvimiento de investigaciones con mejor delineamiento y rigor metodológico, produciendo fuertes evidencias relacionadas al tema investigado

DESCRIPTORES: Cuidado de enfermería; Hipodermoclysis; Infusiones Subcutáneas; Reacción en el punto de inyección.

INTRODUCTION

In Palliative Care, oral medication administration is used because it is the simplest and least invasive route.¹ In cases where the oral route is not feasible, other routes should be considered. Studies have reported that up to 70% of patients facing life-threatening diseases will need an alternative route for oral administration of medication, usually due to reduced level of consciousness and inability to swallow.¹

In these situations, the subcutaneous route presents itself as an option for drug and fluid administration when the oral route is contraindicated, especially for patients with dysphagia, persistent nausea and vomiting, intestinal obstruction, constipation, and diarrhea, allowing the correction of dehydration that does not require prompt volume replacement.¹ Patients with mental confusion and severe dyspnea may also benefit from the use of this route of administration.^{1,2}

Thus, hypodermoclysis, which consists of administering fluids and medications subcutaneously, is less traumatic and provides comfort to patients in the final stages of the disease.² This route of administration is indicated for patients with fragile venous network and dehydration. In addition, it is low cost, presents a variability of sites for its application, and can be used in both hospital and home care.³

The limitations of this route are in relation to volume and speed, and it is contraindicated for patients who have a rapid

need for volume replacement, i.e., in situations such as severe dehydration and volume shock.¹

Among the complications mentioned in literature for hypodermoclysis are pain and edema at the puncture site, cellulitis and insufficient absorption of the solution with accumulation of fluid at the site.⁴ These complications are considered simple for not bringing great harm to patients, however, they cause discomfort to the patient under Palliative Care.

However, hypodermoclysis is still underused and little diffused as an alternative for the administration of fluids and medications, which may negatively influence the patient's quality of life.

In this sense the objective of this study was to identify evidences in literature about the local complications of the use of hypodermoclysis in patients under Palliative Care.

METHODS

This is a systematic review, a method that allows the synthesis of multiple published studies.⁵

When complications or adverse effects of hypodermoclysis are evaluated, two types of complications may present themselves, namely: 1) local and regional complications at the catheter insertion site and 2) systemic complications. For this study, the first type was chosen, as they are the most prevalent and present gaps in scientific evidence in a systematic way.⁶

The following guiding question was formulated: What is the evidence regarding local complications of hypodermoclysis in palliative care patients?

To guide the search, the PICO strategy was used,⁷ in which the letter P refers to patient (palliative care patients), I to intervention (hypodermoclysis), C to comparison (comparison with other interventions was not used as a search strategy) and O to outcome/outcomes (complications, local adverse effects at the puncture site). Searches were conducted from November to December 2020.

The studies were obtained from public domain accesses of the journals portal of the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), in the Medical Literature Analysis and Retrieval System Online (MEDLINE®) databases via PubMed, Latin American and Caribbean Literature on Health Sciences (LILACS), Nursing Database (BDENF), and in the virtual library Scientific Electronic Library Online (SciELO), using the advanced search method. In addition, studies found by means of manual search in other sources, such as free search in Google Scholar and reverse search, provided they met the inclusion criteria.

The following descriptors were used with the aid of Boolean connectors: hypodermoclysis OR “Subcutaneous Infusions” OR “Subcutaneous Absorption AND “Drug-Related Side Effects and Adverse Reactions” OR “Side Effect” OR “Adverse Effects” OR “Adverse Reaction”. The search in English language bases was performed with the following Medical Subject Heading (MeSH) terms: “hypodermoclysis” OR “Infusions, Subcutaneous” OR “Subcutaneous Absorption” AND “Drug-Related Side Effects and Adverse Reactions” OR “Adverse Drug Event” OR “Adverse Drug Reaction” In the Capes database, only the descriptor hypodermoclysis OR “Subcutaneous Infusions” OR “Subcutaneous Absorption” was used.

For data collection, the authors prepared an instrument developed in Microsoft Word program. It included the following variables: authors, type of study and level of evidence, and main results and conclusions. The level of evidence was assessed using the Oxford Centre for Evidence Based Medicine instrument.⁵

Inclusion criteria were: primary studies that addressed hypodermoclysis or subcutaneous infusion in Palliative Care patients, presenting as an outcome the presence of complications or adverse effects resulting from hypodermoclysis, published until November 2020, with restriction to Spanish, Portuguese and English languages. Exclusion criteria were: literature reviews (narrative, integrative and systematic), conceptual studies and articles developed in animals.

Studies that met the inclusion criteria and answered the research question were selected for full analysis. The studies were analyzed by four researchers, two of whom were specialists in the subject and in research methods, and the other two were previously trained nursing academics.

The analysis and selection of the studies were carried out in three phases. In the first, carried out by three researchers, the studies were analyzed and pre-selected, according to the inclusion and exclusion criteria by reading the titles and abstracts, and when these were not available, by reading the full article.

After the pre-selection, the studies were read and fully analyzed with the aid of the data collection instrument, built by the researchers, including: type of investigation, objectives, sample, method, outcomes, results, and conclusion. The third phase included the evaluation of the studies by the four researchers independently, aiming at the objectives of this integrative review, arriving at the studies selected for the research. For the selection of publications, the recommendations of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) cited by Moher et al.⁸ (Figure 1) were followed.

RESULTS

From the database search and reverse search, 374 articles were retrieved, and after adopting the inclusion criteria, 53 articles were selected for reading in full. After this step, 16 studies were considered eligible for analysis and discussion in this study.

Regarding the year of publication of the articles, the oldest dates back to 1994 and the most recent to 2017. Most of the articles (56%) were published in the last ten years. The number of participants involved in the study evaluations ranged from 10 to 96 patients and the study period, most (64%) ranged from 6 to 12 months.

The most used study type was cohort, observed in 68.75% of the studies, followed by Randomized Clinical Trials (RCT – 25%). The most reported level of evidence was 2B (50.0%) and 1B (43.75%) (Chart 1). The average age of the patients recorded in the studies, in all articles, is above 60 years of age (Chart 1).

Among the local complications caused by hypodermoclysis, the studies point out a variation of 3.2% to 32.2% in patients presenting some type of complication, the most frequently cited being erythema, edema, cellulitis, leakage and pain (Chart 1).

Needled and non-needled catheters were the most used in the studies evaluated, with numbering ranging from 21 to 27. Only one study used the jelco, with numbers ranging from 20 to 24. Different infusion sites were recorded, the most cited being femoral, abdominal, infraclavicular. The catheter change time verified in the studies ranged from 1 to 10 days. Only 4 articles cited the use of hyaluronan/UTR and the type of coverage of the infusion site (Chart 2).

Among the solutions and medications that are administered via hypodermoclysis, sodium chloride, glucose, potassium chloride, opioids, anticholinergics, antiemetics, antipsychotics, among others, which are given continuously or as boluses, stand out (Chart 3).

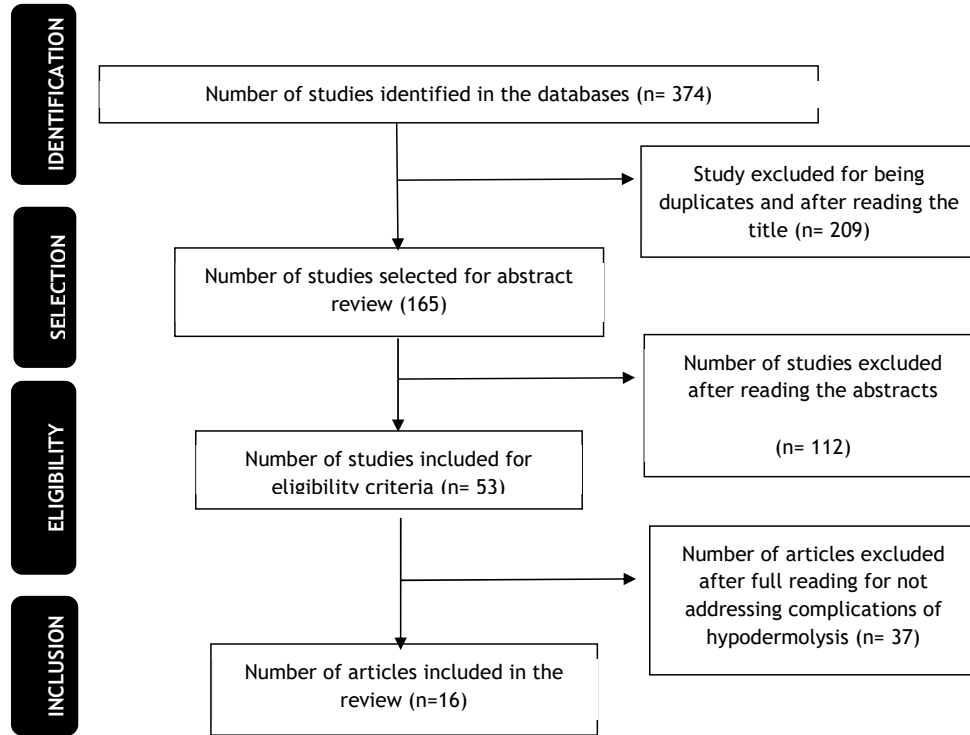


Figure 1 – Flowchart of identification and selection of studies from the systematic review. Belo Horizonte, MG, Brazil, 2020
 Source: Adapted from Moher et al.⁸

Chart 1 – Characterization of the primary studies of the review. Belo Horizonte, MG, Brazil, 2020

	Authors	Year	Goal	Type of study/ level of evidence	Age	Local complications
E1 ⁹	Slesak et al.	2003	Compare the acceptability and feasibility of the SC and IV routes and compare the side effects and clinical parameters of both routes in dehydrated elderly patients	RCT/evidence level 1B	>60 SC:85,3±7,6 IV:85,3±5,8	SC: 48 patients >10 cm Edema: 16.6%. erythema: 4.2% cellulitis: 2.0%. <10 cm Leakage: 14.6%. Erythema: 16.6% Edema: 22.9% Mild pain: 12.5% Hematoma: 14.5% Pruritus:2,0% Obstruction: 2.0%. IV: 48 patients >10 cm Edema: 14.5% Erythema: 4.2% Cellulitis: 2.0% Phlebitis and pain: 2.0%. <10 cm Leakage: 31.2% Edema: 8.3% mild pain: 14.6% Hematoma: 8.3% Phlebitis: 10.4%.
E2 ¹⁰	Noriega et al.	2014	To evaluate the non inferiority of the SC route compared to the IV route in the elderly with dehydration	RCT/evidence level 1B	SC:86,4±8,5 IV:84,3±6,6	SC: 34 patients Edema: 14.7%. Cellulitis: 2.9%. IV: 33 patients Edema: 6.0% phlebitis: 6.0%.

Chart 1 – Cont.

	Authors	Year	Goal	Type of study/ level of evidence	Age	Local complications
E3 ¹¹	Challiner et al.	1994	Compare the effectiveness of SC and IV administration as hydration therapy in elderly patients with acute stroke	RCT/evidence level 1B	SC:82,8 IV:84,2	SC: 17 patients Erythema: 11.7%. IV: 17 patients Hematoma: 5.8%.
E4 ¹²	Zaloga et al.	2017	Compare the efficacy and safety of SC administration of parenteral nutrition with the IV route	RCT/evidence level 1B	SC:84,4±6,1 IV:84,9±5,9	SC: 32.2% (19/59) Edema >10 cm: 22% Erythema: 8.5% (19/59) Cellulitis: 1.7% (9/61) IV: 14.7% (9/61) Edema >10 cm: 8.2% Erythema: 3.3% Pain: 1.6% Cellulitis: 1.6% iv: 14.7% (9/61) Pain: 1.6% Cellulitis: 1.6% iv Change of route: 34.4% (9/61)
E5 ¹³	Bruera et. al.	1990	To describe the experience with hypodermoclysis for the administration of fluids, electrolytes and drugs in cancer patients	Concurrent cohort/ Level of evidence 1B	SC: Regular 62±14	6,9% (4/58) Infection: 3.4% (4/58) Hematoma: 3.4% (4/58)
E6 ¹⁴	Arinzon et al.	2004	To evaluate the clinical benefits of hypodermoclysis in hospitalized patients	Concurrent cohort/ Level of evidence 1B	SC: Regular 78,2±7,2	12% (7/57patients) Erythema: 1.7%. Edema: 5.3% Edema + pain: 5.3%
E7 ¹⁵	Perera et al.	2011	Demonstrate the feasibility of SC hydration. Update the technique and learn about the difficulties and possible complications	Concurrent cohort/ Level of evidence 2B	SC: Regular 69,7 (52-75)	Edema: NI Pain: NI
E8 ¹⁶	Justino et al.	2013	To describe the applicability of hypodermoclysis in patients oncológicos de CP	Concurrent cohort/ Level of evidence 2B	SC: 61 (22-95)	10% (3/30 sites) Irritation: 6.7%. Hematoma: 3.3%.
E9 ¹⁷	Dasgupta et al.	2000	To evaluate hypodermoclysis as a treatment in residents with decreased oral intake. To compare hypodermoclysis with the IV route in the treatment of mild to moderate dehydration	Concurrent cohort/ Level of evidence 2B	SC:83,7±10,5 (52-100)	Edema, Erythema, and Obstruction. SC: 0.05±0.10 IV: 0.20±0.25
E10 ¹⁸	Baudron et al.	2017	Describe the adverse effects and risk factors associated with hypodermoclysis	Concurrent cohort/ Level of evidence 1B	SC: Regular 83±12,5	25.3% (68/269 patients) Pain: 11.0%. Hardening: 7.0%. Erythema: 2%. Hematoma:6.0%
E11 ¹⁹	Mitchell et al.	2012	To investigate the correlation between medications administered via SC through a syringe driver and the incidence of complications at the site	Concurrent cohort/ Level of evidence 2B	SC: Regular 72 (61–79)	Needle catheter: 54 sites Leakage: 1.8%. Bleeding: 27.7%. Bruising: 3.6%. Hardening: 16.7%. Erythema: 9.3% Others: 12.9% Not mentioned: 24.1%. Non needed catheter: 7 sites Bruised: 14.2% Hardening: 57.1% Erythema: 28.6 %
E12 ²⁰	Pirrello et al.	2007	To describe the experience of using hyaluronidase in solution and drug infusion	Non-competing cohort/ Level of Evidence 2B	SC: Regular 69,7(39-98)	15% (5/32 records) Hematoma: 12.5%. Hardening: 3.1%.
E13 ²¹	Pino et al.	2011	Describe the use of the SC route in palliative care at the end of life	Non-competing cohort/ Level of Evidence 2B	SC: (65-95)	4,5% (1/22) Erythema: 4.5% (1/22)

Chart 1 – Cont.

	Authors	Year	Goal	Type of study/ level of evidence	Age	Local complications
E14 ²¹	Yap et al.	2001	Review the use of hypodermoclysis in a local hospital	Non-competing cohort/ Level of Evidence 2B	NI	34.2% (27/79 sites) Erythema: 16.4%. Extravasation: 15.2%. Bleeding: 2.5%.
E15 ²²	Rémi et al.	2014	To evaluate the effectiveness and tolerability of SC leviratizetam for epileptic seizure in CP	Non-competing cohort/ Level of Evidence 2B	SC: Regular 69 (42–82)	3.2% (3/93patients) Immediate hyperemia:1.0%. Hyperemia:2.0% 4 to 6 days
E16 ²³	Neo et al.	2016	Compare the complications of using metal needles and plastic cannulas	Observational study/ Level of evidence 2C	SC:67,7–9,5	29.6% (8/27 patients) Pain: 3.7% (8/27 patients) hematoma: 3.7% (8/27 patients) Erythema: 3.7% (8/27 patients) Hematoma:11,1%

ECR: Randomized Clinical Trials; SC: Subcutaneous; IV: Intravenous; NI: Unidentified.

Source: Prepared by the authors

Chart 2 – Clinical factors related to the hypodermoclysis puncture procedure. Belo Horizonte, MG, Brazil, 2020

	Catheter type and catheter number	Infusion site	Catheter changing time (days)	Use of hyaluronidase/UTR	Covering at the infusion site
E1 ¹²	SC: Needled n° 21 IV: n° 22	Femoral, abdominal, infraclavicular	SC: 2 (0,5; 9) IV:2,8 (0,3;8,8)	Yes 150	Transparent tape
E2 ¹³	SC: Needle No. 21 to 25 IV: Jelco n° 20 to 24	SC: Femoral, abdominal, scapular. IV: Dorsal hand, forearm, elbow flexion	NI	NI	NI
E3 ¹⁴	Needlepointed and non-needlepointed	Infraclavicular, scapular, femoral	NI	1500	NI
E4 ¹⁵	NI	NI	NI	No	NI
E5 ¹⁶	Needled n° 25	Abdominal, infraclavicular	4±3	Yes 750	NI
E6 ¹⁷	Not Needled n° 21	Femoral	1	No	Occlusive dressing
E7 ¹⁸	Agulhado n° 23 ou 25	Infraclavicular, deltoide	3 to 6 avarage 1–10	NI	Transparent tape
E8 ¹⁹	Agulhado n° 21 a 27	Infraclavicular 93%, Abdome 7%	Up to 7	NI	NI
E9 ²⁰	NI	NI	NI	NI	NI
E10 ²¹	Needled Not Needed	Abdominal, femoral	NI	No	NI
E11 ²²	Needled and Not Needed	NI	Needled: 2 (1-4) Teflon: 2 (1-5)	No	NI
E12 ²³	Needled n° 22 a 24	Abdominal, femoral, infraclavicular, deltoid	NI	Yes 150	NI
E13 ²⁴	NI	Infraclavicular	NI	NI	NI
E14 ²⁵	Needled n° 23 to 25	Abdominal, interescapular	3 d	NI	Transparent tape
E15 ²⁶	Needled	NI	NI	No	NI
E16 ²⁷	Needled n° 23 Not Needled n°4	Deltoid and abdominal	Needlepointed: 2.5 Not needed: 3-4	NI	NI

SC: Subcutaneous; IV: Intravenous; RTU: Turbidity Reducing Unit; NI: Not identified.

*Studies E3, E10, E11 and E15 did not specify the catheter number used.

Source: Prepared by the authors

Chart 3 – Factors related to the process of drug administration via hypodermoclysis. Belo Horizonte, MG, Brazil. 2020.

	Solutions	Management Type	Medications	Volume at infusion site/day
E1 ⁹	NaCl 0,9%, G 5% KCl 24 mmol/L	Bolus	NI	SC: 750 (457;1,500) mL/d IV:1,000 (500;1,500) mL/d
E2 ¹⁰	NaCl 0,9%, G 5% KCl 20 mEq	NI	NI	SC:1,320 ml±400 ml IV:1,480 ml±340 ml
E3 ¹¹	NaCl 0,9%, G 5%	Continuous	SF 0,9%, glucose 40 g	2000 ml every 24 hours
E4 ¹²	Parenteral nutrition.	Continuous	Parenteral Nutrition	NI
E5 ¹³	NaCl 0,9%, G 5%, KCl	Continuous	Opioids	1,3L±0,8
E6 ¹⁴	NaCl 0,9%, G 5% e 3%	Continuous	Not administered	1161±197
E7 ¹⁵	NaCl 0,9%, G 5%	Continuous and Intermittent	NI	1000 ml
E8 ¹⁶	NaCl 0,9%, G 5% and 50% Electrolytes	Bólus	Opioid, antiemetic, diuretic; non-opioid analgesics; antispasmodic, anticholinergic	NI
E9 ¹⁷	NaCl 0,9%, G 5%	NI	NA	NI
E10 ¹⁸	NaCl 0,9%, G5%, Double distilled water	Bólus	Antibiotics	NI
E11 ¹⁹	NaCl 0,9% Double distilled water;	Continuous	Antiemetic, antipsychotics, antipsychotics, opioids, antipsychotics	NI
E12 ²⁰	NaCl 0,9%, G 5% KCl, Mg	Continuous	Opioids, non-opioid analgesic, corticoid, antipsychotic, benzodiazepine, antiemetic, proton pump inhibitors	NI
E13 ²¹	NaCl 0,9%	Continuous	Opioid, anticholinergic	500 to 1500cc in 24 hours
E14 ²²	NaCl 0,9%, G 5%, KCl 2g	NI	NI	1,5L in one place and up to 3L in two places (1L at night)
E15 ²³	NI	Continuous	Anticonvulsant, benzodiazepines, opioid, anticholinergic, antiemetic, corticoid, antipsychotic, anti-hypertensive	NI
E16 ²⁴	NI	Bólus	Opioid, anticholinergic, antiemetic, antipsychotics	Metal cannula: 2.4-28.9 ml/h Non-needle: 2-60 ml/h

NaCl: sodium chloride; G: glucose; KCl: potassium chloride; Mg: magnesium; NI: not informed.

*E8 does not describe the electrolytes

Source: Prepared by the authors

DISCUSSION

After critical analysis of the selected studies, relevant information was selected and grouped into three categories: characterization of the studies and complications; factors related to the hypodermoclysis procedure and factors related to solution and drug administration.

Characterization of the studies and complications

Regarding the object of study, of the four RCTs verified, three compared the use of SC therapies with IV for hydration,^{9,10,11} and one compared the efficacy and safety of SC administration of parenteral nutrition with the IV route.¹² In the observational studies the objects of study were diverse, such as to describe, evaluate and analyze the use of hypodermoclysis,^{13,14,15,16,21,22}

compare the use of SC and IV therapies for hydration,¹⁷ compare the use of needled and nonneedled catheters in the incidence of complications²⁴ evaluate the feasibility of administering drugs through the SC route, such as antibiotics, diuretics, sedatives and antiepileptic drugs,^{18,19,23} besides describing the use of hyaluronidase in solution and drug infusion.²³ Although some studies^{18,19,23} show the safety and efficacy for the different classes of drugs when applied subcutaneously, more studies are needed to elucidate their complications.

One aspect that draws attention is the small number of RCTs related to the subject. As for the level of evidence, the four RCTs^{9,10,11,12} were evaluated as high quality, meaning that they can be used as a source of evidence to guide clinical practice. In the observational studies, most of the studies were classified as level of evidence 2B.

The age bracket studied comprises the elderly population, i.e., its major use is in geriatric patients and at the end of life.¹ In this age bracket and health condition, there is greater fragility of the venous network and less possibility of invasive interventions, which enables its greater use in this public.

Local complications such as edema^{9,11,12,13,14,15,17} and erythema^{16,21,22,23} were the most prevalent, however, in RCTs this result was not statistically significant.^{9,10,11,12} Importantly, edema presents as a complication, without changes in therapeutic attitudes or worsening of the clinical picture, being solved by changing the infusion point, i.e., a new puncture.¹² Erythema is easily resolved, since, after removal of the device introduced into the SC tissue, the signal dissipates after a few hours.^{21,22} Moreover, the use of the SC route presents complications at the site of catheter insertion that can be avoided with adequate management of the technique, among them the daily observation of the puncture site and follow-up of the patient's response.

Factors related to the hypodermoclysis procedure

The technique of subcutaneous infusion of solutions and drugs occurs by inserting a device in the subcutaneous tissue.¹ The puncture can be performed with both types of catheter, needled (scalps)^{9,10,11,13,15,16,20,22,23} and non-needled.¹⁴ In four studies both catheters were used.^{14,21,22,27} It is known that the non-needled type brings less discomfort to the patient, besides increasing catheter dwell time.^{9,24} However, the lower cost of the needled catheter may influence its adoption in clinical practice,^{9,12,24} as was evidenced in the present study.

It is important to consider that when comparing drug administration with the two types of catheters, it was observed that there was a greater reaction at the puncture site (26.5%) when the needled catheter was used in relation to the non-needled catheter (7.7%) with Teflon cannula.^{19,24}

The size of the needled catheter indicated to perform the hypodermoclysis technique varies from 21G to 25G and non-needled from 20G to 24G, with preference for the smaller size considering that it does not influence the absorption of drugs,^{1,25} however, it is believed that the size of the catheter influences the occurrence of complications, because it can cause obstruction due to the smaller size.

The topographical regions for the puncture site differ in relation to the maximum amount of volume that each one is capable of receiving over 24h, thus, among the infusion sites most cited in the studies were the femoral region,^{9,11,12,14,18,20} abdomen,^{9,11,13,16,18,20,23,24} infraclavicular,^{9,11,13,15,16,20,21} scapular^{10,11,22} and deltoid.^{15,20,24} The puncture sites were not reported in four studies.^{12,17,19,23} It should be noted that the tolerance of each region for infusion of solutions and drugs varies according to the volume and general conditions of the patient.¹

Most studies do not report the catheter dwell time,^{10,11,14,17,18,20,21,23} in the studies that have this information, the mean time ranged from two to four days in those that used the needled catheter,^{9,13,15,19,22,24} from one to two days for the non-needled catheter.^{14,19}

The authors report that the reason for withdrawal for both types of catheter was due to the presence of local complications at the insertion site and discontinuation of therapy, with the exception of the study,¹⁴ in which the length of stay was one day with non-needled catheter, the reason for withdrawal is not mentioned. It is believed that it may be due to compliance with institutional protocols. In the study¹⁶ does not report the average length of stay, but mentions that in the absence of complications the needled catheter was removed after the seventh day.

Although four studies used hyaluronidase to improve the absorption of drugs and solutions into the subcutaneous tissue, at a dose of 150 Turbidity Reducing Unit (TRU),^{9,19} 1500 TRU¹¹ and 750 TRU¹³, edema and hematoma prevailed as complications in these studies.

Of the studies analyzed, only four mentioned the type of cover used, being transparent cover,^{9,22} gauze¹⁴ and adhesive tape.¹⁵ Fixation of the catheter at the puncture site, preferably, should be performed with sterile and transparent cover, because it allows visualization and monitoring of the puncture site.¹

Factors related to the administration of drugs and fluids

Administration of fluids and drugs subcutaneously involves indications from solutions for hydration maintenance to drug infusion for relief of symptoms such as pain, nausea and vomiting, intestinal obstruction, infections.^{1,26}

Among the solutions used, all studies used 0.9% NaCl, 11 studies used 5% glucose,^{9,10,11,13,14,15,16,17,18,20,22} one used 3% glucose¹⁴ and another used 50% glucose.¹⁶ The 5% glucose solution is considered isotonic, i.e., safe for subcutaneous use.¹ On the other hand, 50% glucose may cause complications due to its hypertonicity. Potassium chloride (KCl) was the electrolyte most often used,^{9,10,13,20,21} and it can be administered as long as diluted in 0.9% saline solution or 5% glucose solution, with the purpose of reducing pain or irritation at the infusion site.¹ Magnesium was reported in one study²⁰ and the type of electrolyte was not mentioned in the studies.^{16,24} It is important to note that the SC route was also used for infusion of nutritional diet¹¹ and in this case, the authors reported that the osmolarity of the diet was 845 mOsm/l, in this sense, the recommendation is that the osmolarity does not exceed 300 mOsm/kg, i.e., the diet used in the study is considered with high osmolarity for infusion via SC.^{1,27}

With regard to the drugs used, opioids,^{13,16,19,20,21,23,24} antipsychotics,^{19,20,23,24} non-opioid analgesics,^{16,20} anticonvulsants, corticoids and hypertensives,^{20,23} antispasmodics and diuretics¹⁶ and antibiotics prevailed.¹⁸ It is known that water-soluble drugs and those with a pH close to neutrality are compatible with the subcutaneous route.^{1,25,27} It is reported that the occurrence of complications at the insertion site, such as erythema, may be associated with the osmolarity of the administered drugs,^{19,23} so their administration should be slow and careful.²³

Pirrello et al.²⁰ report that there is little information on the effects of drugs when used via SC. In three studies,^{14,15,17} the SC

route was used only for hydration, which is why the use of medications was not identified and the study lacks this information.²²

Administration of solutions and drugs was continuous, that is, with the application of an infusion pump,^{13,14,15,19,20,21,22,23} in bolus,^{16,18,24} continuous and intermittent,¹⁸ and the type of infusion was not described in the study.¹⁷

The volume infused at the puncture sites did not exceed 1500 mL/24 hours,^{9,10,13,14,15,21,22,24} except in the study¹¹ which reported 2000ml/day. In situations where infusion of a greater volume of solution/medication was necessary, a new site should be punctured.²² The remaining seven studies did not describe the daily volume infused.^{11,16,17,18,19,20,23}

A minimum infusion rate of 20 ml/h and a maximum of 100 ml/h was adopted in the studies,^{13,14,15,17,24} from seven to ten drops per minute,²¹ in bolus for the infusion of antibiotics, divided into fast (less than 5 minutes) and slow (more than 5 minutes), since some classes of antibiotics, when given rapidly are associated with local necrosis-like complications;¹⁸ the smallest infusion volume was 2ml/h for drug administration,²² the infusion speed was left to the discretion of the nurses²² and in two studies^{16,19} this information was not described by the authors. In the study²⁴ infusion speed was not mentioned.

In view of the studies analyzed, it can be concluded that, although hypodermoclysis is an old technique, there are still questions about the factors that can influence the complications resulting from this route, which prevents its wide adoption for patients in palliative care.

It is pointed out that limitations occurred in this study, due to the method used in the selected studies, a lack of information on important variables that may trigger complications at the catheter insertion site is identified. Further studies are suggested on the association between clinical factors, the technique and infusion of solutions and drugs with the presentation of complications.

CONCLUSION

From the results, the following evidences were identified: the most prevalent complications resulting from the use of hypodermoclysis were edema and erythema. Regarding the factors related to technique, the use of needled catheter predominated, the abdominal and infraclavicular regions were the most used, the catheter permanence time varied from one to ten days. Hyaluronidase was used in varying doses. Only two studies reported the use of a transparent cover for catheter fixation. In factors related to the administration process of solutions and drugs, NaCl 0.9% was used in all studies and the main electrolyte is KCl; opioids were administered in most studies, by continuous infusion and infusion volume lower than 1500ml, whose infusion speed ranged from 20 to 100 ml/hour

From the analysis of the studies included in this review, it is understood that there is a need to intensify efforts to develop research with better design and methodological rigor, producing strong evidence on the subject investigated.

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