ABSTRACT

Objective: To describe the evidence available in the literature about the knowledge and practices of subcutaneous fluid administration in cancer patients. Methodology: Integrative literature review, using the keywords nursing, hypodermoclysis, subcutaneous therapy, and cancer; in English, Portuguese and Spanish, with no publication deadline. Of the 160 articles found, 11 comprised the sample. Results: Of these articles, 54% (n = 6) were published in the English language, 63% (n = 7) were published in the last five years. Among them, 81% (n = 9) are classified with the level of evidence six because they are observational studies or reports of experiences, while two studies are literature reviews. As for the main subject of the studies, most research points to the use of the subcutaneous route in patients under palliative care at home. Conclusion: In this research, it was possible to know hypodermoclysis, its indications, purposes, advantages, and disadvantages, concluding, from the studies analyzed, that this route of administration of fluids and/or drugs is a possibility of use in cancer patients, with an emphasis on palliative care patients.

Descriptors: Nursing, hypodermoclysis, cancer, subcutaneous tissue, pharmacological treatment.

RESUMO

Objetivo: Descrever as evidências disponíveis na literatura acerca dos conhecimentos e das práticas da administração de fluidos por via subcutânea em pacientes oncológicos. Metodologia: Revisão integrativa de literatura, utilizando os descritores enfermagem, hipodermóclise, terapia subcutânea e câncer; nos idiomas inglês, português e espanhol, sem data limite de publicação. Dos 160 artigos encontrados, 11 compuseram a amostra. Resultados: Destes artigos, 54% (n=6) estavam publicados na língua inglesa, 63% (n=7) foram publicados nos últimos cinco anos. Dentre eles 81% (n=9) são classificados com nível de evidência seis por constituírem estudos observacionais ou relatos de
experiências, enquanto dois estudos são revisões de literatura. Quanto ao assunto principal dos estudos, a maioria das pesquisas aponta a utilização da via subcutânea em pacientes em cuidados paliativos domiciliares. **Conclusão:** Nesta pesquisa foi possível conhecer a hipodermoclise, suas indicações, finalidades, vantagens e desvantagens, concluindo, a partir dos estudos analisados, ser essa via de administração de fluidos e/ou fármacos uma possibilidade de uso em pacientes oncológicos, tendo como ênfase nos pacientes em cuidados paliativos.

**Descritores:** Enfermagem, hipodermoclise, câncer, tecido subcutâneo, tratamento farmacológico.

**RESUMEN**

**Objetivo:** Describir la evidencia disponible en la literatura sobre el conocimiento y las prácticas de la administración de fluidos subcutáneos en pacientes con cáncer. **Metodología:** Revisión integrativa de la literatura, utilizando las palabras clave enfermería, hipodermoclisis, terapia subcutánea y cáncer; en inglés, portugués y español, sin fecha límite de publicación. De los 160 artículos encontrados, 11 componen la muestra. **Resultados:** De estos artículos, 54% (n = 6) fueron publicados en idioma inglés, 63% (n = 7) fueron publicados en los últimos cinco años. Entre ellos, el 81% (n = 9) se clasifican con nivel de evidencia seis porque constituyen estudios observacionales o relatos de experiencias, mientras que dos estudios son revisiones de literatura. En cuanto al tema principal de los estudios, la mayoría de las investigaciones apuntan al uso de la vía subcutánea en pacientes en cuidados paliativos domiciliarios. **Conclusión:** En esta investigación se pudo conocer la hipodermoclisis, sus indicaciones, propósitos, ventajas y desventajas, concluyendo, a partir de los estudios analizados, que esta vía de administración de líquidos y/ o fármacos es una posibilidad de uso en pacientes oncológicos, con un énfasis en los pacientes de cuidados paliativos.

**Descritores:** Enfermería, hipodermoclisis, cáncer, tejido subcutáneo, tratamiento farmacológico.

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INTRODUCTION

Organization (WHO), in 2017, cancer is recognized as one of the main causes of global morbidity and, therefore, a growing concern for public health, with the annual number of new cancer cases carcinogens increase from 14.1 million in 2012 to 21.6 million by 2030\(^1\).

Despite investments in new research in oncology, treatment is still based on three aspects: surgery, chemotherapy, and radiotherapy. These therapies can be used as monotherapy or concomitantly, with the purpose of a better response, considering the type of tumor, staging, and performance status of the patient\(^2\).

Among the three types of treatment, chemotherapy is still the most used, as it has a systemic action, intending to treat it as present micrometastases. It is usually administered through the peripheral venous network, it has drug characteristics that can be irritating and/or vesicating, with effects on the venous network, with chances of the patient evolving with a compromised peripheral network, thus requiring other fluid administration routes. and/or drugs\(^3\).

Another administration mechanism is hypodermoclysis, which is defined as the administration of fluids in the subcutaneous space in a continuous or intermittent way\(^4\). The use of this route was charged in 1914 for the hydration of pediatric patients. More than three decades later, in 1950, this technique fell out of favor due to iatrogeny related to the quality of the puncture and the solutions administered. Likewise, due to advances in technology, hypodermoclysis was abandoned around 1950, with serious complications related to fluid overload and circulatory shock, after large volume infusions by the subcutaneous route (SC)\(^5\).

Around the 1980s, hypodermoclysis was again applied in the literature in England, being used in elderly patients and palliative care, then reassessed as a way of administering drugs safely. Emphasized regarding volume restrictions, medications that the subcutaneous tissue tolerates, as well as the puncture technique and nursing care with the route\(^6\).

The hypodermis is also known as subcutaneous tissue (SC), having as its main function the nutrient deposit of energy reserve, in addition to the function of end insulator and mechanical protection. It has blood vessels, lymphatic vessels, glands, and nerves. It can be moved by its characteristic of being loose fabric. In this way, it allows it to become a favorite route in the administration of fluids and drugs since these are absorbed and transported to the macrocirculation\(^7\).

The absorption of large volumes of solutions administered by hypodermoclysis and mediated by simple diffusion to blood capillaries and lymphatic vessels, through the action of hydrostatic and
osmotic solutions that allow the solution to reach vascular spaces. However, this absorption is slow, being urgently contraindicated, when you need quick and immediate solutions administered8. Plasma levels are similar to those achieved with intramuscular (IM), oral, rectal, sublingual, and intravenous (IV) administration. The doses of the medications are similar to those of the EV, but the onset of action is similar to that of the oral route, about 15 to 30 minutes after administration5.

Another characteristic is that the vascularization of the SC pathway is only 6% of the cardiac output. Affecting the minor serum limitation, but with a longer duration of action and longer than that of the EV and IM pathways, thus avoiding pre-systemic clearance by the liver, resulting in a stable serum concentration of the drug, to avoid undesirable side effects as a result of plasma peaks5.

The drugs used by this route, do not always have the description of the forecast to be used in the package leaflet, being then administered off-label. The most used drugs are opioid and non-opioid analgesics, antimicrobials, among others6.

For these reasons, it is justified to carry out this integrative literature review, to seek in scientific productions the possibility of using hypodermoclysis in cancer patients, either for hydration and/or for the administration of drugs at the hospital or home level. That said, the study has the following guiding question: What is published in the literature about the use of hypodermoclysis as a possibility in the administration of fluids in cancer patients?

**OBJECTIVE**

The aim of the study is to describe the evidence available in the literature about the knowledge and practices of subcutaneous fluid administration in cancer patients.

**METHOD**

This is an integrative literature review study with a qualitative approach. This method includes the analysis of studies that provide support for decision making and improvement of clinical practice, allowing the synthesis of multiple published studies, to enable general conclusions regarding a certain area of knowledge6.

An integrative review is also one of the methods used in evidence-based practice (EBP), which allows the incorporation of evidence into clinical practice. The use of these requires skills of the health professional, as it requires associating results from research in clinical practice to solve problems.

Thus, the steps described by Mendes, Silveira, and Galvão (2008) were used as a methodological path, according to which, for the construction of the review, it is necessary to strictly follow the six stages of construction of the study, namely: establishment of the hypothesis of study;
sampling or literature search; categorization of studies; evaluation of the studies included in the research; interpretation of results and discussion; and presentation of the review.

Following the methodological rigor proposed for this research, the following question was raised: in what state are the scientific productions about the knowledge and practices that have been used subcutaneously in cancer patients? This questioning was based on the hypothesis that hypodermoclysis is an underutilized therapy by nursing due to the lack of knowledge on the subject.

Figure 1. Articles selected for review, based on the PRISMA.

Then, the literature search was carried out by the researchers in the period from March to April 2020. Therefore, this occurred separately between the authors and, in the last stage, there was a meeting to check the final sample. In case of divergence, the articles were analyzed, resulting in a consensus. The data were collected from the bibliographic bases of the Virtual Health Library (VHL) and the PUBMED portal.

The sampling defined for this research was based on the following inclusion criteria: articles available in full; Portuguese, English, or Spanish language; without time limit for publication. The exclusion criteria selected were: thesis, dissertation, texts that were not contingent on the research
or that did not answer the hypothesis. It is noteworthy that the open time frame was necessary for the view of the difficulty in obtaining articles related to the theme. In each database, the search was carried out in two moments, with the following crossings: first use the subcutaneous therapy descriptors; nursing and cancer, then the data were crossed with the descriptors of hypodermoclysis, nursing, and cancer. AND was the Boolean operator used in the research.

In the PUBMED database, 06 manuscripts were found using the descriptors Hypodermoclysis, Nursing, and cancer; one hundred and forty-two manuscripts with the keywords subcutaneous therapy, nursing, and cancer. Of these, sixty-two were not available in full, 10 were duplicated in the database, twenty-seven were editorials, being excluded from the study.

In the VHL database, 8 manuscripts were found with the descriptors Hypodermoclysis, Nursing, and cancer; and 04 works with the keywords subcutaneous therapy, nursing, and cancer. Of these 12 studies, only 05 were available in full and were included in the analysis.

For the categorization of the studies, it was adopted as a method of data analysis the detailed reading, and the record of the articles that composed the sample. This compilation was summarized using an instrument created by the researchers to summarize the data, with the title of the research, study objective, methodology presented, language, year of the article, journal, basic level, and main findings of hypodermoclysis.

The selected studies are classified the evidence hierarchy system according to Melnyk and Fineout-Overholt10 which provides seven levels of evidence. The articles included were classified into: level 1 - systematic review or meta-analysis of relevant randomized clinical trials; level 2 - evidence obtained from at least one well-approved randomized clinical trial; level 3 - well-designed clinical trials without randomization; level 4 - case-control study and cut-off studies; level 5 - systematic reviews of descriptive and qualitative studies (n = 1); level 6 - single descriptive or qualitative study; and, finally, level 7 - opinion of authorities and/or expert committee. Other studies were not possible to classify as to the level of evidence, as there were methodological studies or literature reviews without method, not covered, because, in the hierarchy of evidence adopted, being classified as not applicable (NA).

As previously mentioned above, the evaluation of the studies included in the research was carried out by the authors and the description of the searches and the selection of articles is summarized in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) (Figure 1). In the course of this analysis, after selecting the sample, the titles of the articles were read, and, if they contained the theme investigated, they were selected to read the abstracts and then the material in its entirety.
After compiling the data, a discussion followed regarding the findings in association with the authors' knowledge on the subject, promoting, finally, a reflection on the use of hypodermoclysis as a therapeutic possibility in the administration of fluids in cancer patients. Therefore, the fifth stage consists of discussing the findings in dialogue with the knowledge gaps on the topic, promoting thinking about nursing. In the sixth stage, we propose the elaboration and formatting of the literature review that is summarized in the results in the form of a table.

We emphasize that the ethical aspects of this research were respected so that the data found in the articles of this review were updated as to origin and integrity.

### RESULTS

In the present study, 11 scientific articles on subcutaneous therapy in cancer patients were analyzed, which strictly followed the sample selection described for this review. The summary of these articles is summarized in a table below, according to authors, year, the language of publication, journal, level of evidence, target audience described in the study, benefits of therapy (Chart 1):

**Chart 1. Distribution of articles included in the research according to the author, year of publication, language, level of evidence, journal, and main results of the study- Fortaleza, CE, Brazil, 2020.**

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Language</th>
<th>Evidence level</th>
<th>Periodic</th>
<th>Target audience</th>
<th>Benefits of therapeutics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breen, m. R. S. C. N. Et al, 2006</td>
<td>English</td>
<td>Level 6</td>
<td>Paediatric nursing</td>
<td>Pediatric oncology patients in home care.</td>
<td>Effective in controlling symptoms such as pain, nausea and vomiting, in the administration of drugs through this route, hospitalizations are unnecessary for symptom control, as well as less painful and allowing greater mobility of the child with the device.</td>
</tr>
<tr>
<td>Vidal, m. Et al, 2016</td>
<td>English s</td>
<td>Level 6</td>
<td>Journal of pain and symptom management</td>
<td>Adult cancer patients in home care.</td>
<td>It implied fewer complications, fewer costs, and the need for little technique, being effective in controlling the patient's symptoms, as well as being cheap for the institution.</td>
</tr>
<tr>
<td>Bartz, l. Et al, 2014</td>
<td>English</td>
<td>Level 6</td>
<td>Cancer pain relief committe</td>
<td>Adult cancer patients in palliative care at home.</td>
<td>It is concluded that it is an effective technique in the administration of drugs for symptom control, it is not costly, but it is not free of complications, requiring a qualified nursing team.</td>
</tr>
<tr>
<td>Name</td>
<td>Language</td>
<td>Level</td>
<td>Journal</td>
<td>Abstract</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
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<td>-----------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Breen, m. 2006</td>
<td>English</td>
<td>Level 6</td>
<td>Paediatric nursing</td>
<td>It was observed the use of hypodermoclysis in children and adolescents in palliative care at home as a possibility of therapy, when the central venous device is not available, being concluded as a viable alternative, less painful, possibility of the varied use of medications to control symptoms in the patient pediatric.</td>
<td></td>
</tr>
<tr>
<td>Marijo, l.; joann, s.; jones, t. D. 1999</td>
<td>English</td>
<td>Level 6</td>
<td>American journal of hospices and palliative care</td>
<td>The study observes the use of the subcutaneous route in the administration of pain medications as an alternative when the oral route is not determined, being considered a safe and effective way to control pain.</td>
<td></td>
</tr>
<tr>
<td>Adams, r. N. 2015</td>
<td>English</td>
<td>Level 6</td>
<td>British journal of nursing</td>
<td>The use of hypodermoclysis was verified in patients with dehydration and concluded as an alternative for rehydration of elderly patients and/or in palliative care who have a difficult venous network.</td>
<td></td>
</tr>
<tr>
<td>Takaki, c. Y. I.; khein, g. F. S. 2010</td>
<td>Portugues e</td>
<td>Level 6</td>
<td>Congientae saúde</td>
<td>Buscou avaliar o conhecimento dos enfermeiros sobre a hipodermóclise. Teve como resultados o baixo conhecimento dos enfermeiros sobre as indicações, a técnica e o manejo da via subcutânea para administração de fluidos. Concluindo que há pouco conhecimento técnico dos enfermeiros sobre uso da compatibilidade e compatibilidade medicamentosa.</td>
<td></td>
</tr>
<tr>
<td>Cardoso, d. H.; mortola, l. A.; arrieira, i. C. O. 2016</td>
<td>Portugues e</td>
<td>Level 6</td>
<td>J nursing health</td>
<td>Experience report on the use of hypodermoclysis in-home palliative care. Seen the route as effective in controlling the patient's symptoms and low cost, as well as the nurses' experience in the applicability of the therapy.</td>
<td></td>
</tr>
<tr>
<td>Author(s) and Year</td>
<td>Language</td>
<td>Level</td>
<td>Journal</td>
<td>Study Title</td>
<td></td>
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</tr>
<tr>
<td>Rodrigues, F. F., et al, 2016</td>
<td>Portuguese</td>
<td>6</td>
<td>Rev enferm ufpe online</td>
<td>The study carried out an intervention with the nursing team of a surgical unit in a hospital, providing permanent education for professionals on the indications and care for the use of hypodermoclysis; considering that, before training, nurses were unaware of the use of the route.</td>
<td></td>
</tr>
<tr>
<td>Bruno, V. G. 2015</td>
<td>Portuguese</td>
<td>Na</td>
<td>Einstein</td>
<td>Literature review. The results found show positive results from the use of the route, but little evidence was found on medications, dilution, ideal dose, etc., showing little information on the most correct way of using medications by this route, even though it is an effective and safe option.</td>
<td></td>
</tr>
</tbody>
</table>

Of the articles that made up the sample, 54% (n = 6) were published in the English language, 63% (n = 7) were published in the last five years and 81% (n = 9) are classified with the level of evidence 06 because they constitute observational studies or reports of experiences, while 02 studies are literature reviews. As for the core of the studies, most research directs the use of the subcutaneous route in patients under palliative care at home. Both pieces of research bring this practice as an effective and low-cost therapy. It is noteworthy that the reviews previously evaluated on the theme likewise showed the low use of the specific technique and the low scientific production in the area. It is also important to highlight the lack of knowledge of the nursing team regarding the possibility of using the route in cancer patients, the technique, and which medications can be administered.

**DISCUSSION**

The number of articles on hypodermoclysis in cancer patients found pieces of evidence that need to expand research on the subject to better understand the therapy as well as its technique, considering the importance of hypodermoclysis in the clinical practice of the nursing team.
It is also observed in the studies that composed the sample, characterized as the level of evidence 6, composed only of observational and/or descriptive studies, demonstrating the need for nurses to carry out expanded clinical studies on the application of hypodermoclysis as a therapy, as well as its advantages and its disadvantages, both at the hospital and home level.

Although the result reveals the prevalence of the English language as the language of choice for publications, with the purpose of not creating a barrier at the academic level of Brazilian students, as well as for professionals working in assistance when encountering some difficulty when consulting about the route in question. their care practice11. Most studies have been developed at an international level, revealing that the use of the route is more explored abroad. Therefore, there is a need to develop further Brazilian studies on the use of the route in cancer patients, due to the large number of patients diagnosed with this pathology and who determines the quality and medical care.

The studies found in Brazil offer greater emphasis on home care, showing the possibility of maintaining symptom control, thus providing greater comfort for patients without requiring prolonged hospitalizations, and may also provide an end of life at home without suffering.

Regarding the main theme of forced studies, most reveal the use of hypodermoclysis in patients in palliative care, this fact is justified by the fact that patients, at this stage of the disease, have unpleasant symptoms such as pain, dyspnoea, nausea, vomiting, dehydration, the impossibility of using the oral route, affecting the quality of life of patients leading to suffering; likewise, due to multiple cancer treatments, patients have a fragile peripheral venous network, requiring an alternative route for flawless symptom control 12,13,14.

The literature brings hypodermoclysis as a possibility of use, requiring the puncture to be performed by a qualified nurse professional and a trained team to maintain the pathway. On average, the catheter via SC is about five to seven days in the same puncture site without showing inflammatory manifestations. A study15 showed the use of the SC route in patients in-home care, resulting in an average of 7.25 days of catheter stay, with the death of the patient being the most prevalent reason for the removal of the device, followed by local complications such as induration, hyperemia, heat, and local edema, having none related to the severe adverse reaction to the medications administered.

The drugs administered in hypodermoclysis are commonly used off-label, that is, their indication does not appear in package inserts or protocols, and is then based on the care practices of the institutions, at the discretion of the prescriber, considering volumes compatible with the puncture site, characteristics of the drugs in terms of pH, since the SC pathway supports drugs with
neutral characteristics due to their absorption if it is based on the principle of simple diffusion. Some 
drugs are contraindicated because they present risks of causing irritation or tissue necrosis, justifying 
in addition to the extreme pH (too acidic or too alkaline), the osmolarity and solubility of the 
formulation or solution, so far, they are described as incompatible with the route: Diazepam, 
diclofenac, undiluted electrolytes and phenytoin⁵.¹⁴.

The drug best described in the literature for use via SC are opioids, its administration is 
considered safe and effective and with few adverse effects due to the reduction of fluctuations in 
the plasma concentrations of these medications, considered one of the advantages of using this 
route¹⁶.

Of this, other advantages are eliminated, including the low cost, by the need to use 
inexpensive materials when compared to other types of punctures, indicating as an example the costs 
of EV therapy, four times higher. The simplicity for insertion of the peripheral catheter, ease of 
administration and maintenance, enabling early discharge from hospital for its effectiveness, with 
safety and ease in handling at home, also promoting comfort, convenience, and autonomy to the 
patient, as well as minimal risk of local and systemic complications¹¹, ¹², ¹³, ¹⁴, ¹⁵.

Not that it concerns the disadvantages, it is cited ¹¹, ¹⁴, ¹⁶ the limitation in the infusion speed, 
when this transfer of liquids occurs at a speed of 1ml / minute, the absorption occurs without edema 
and in the rapid adjustment of the doses since the absorption by the subcutaneous tissue be slower 
when compared to the EV route.

Thus, this route corrects situations in which a rapid infusion and a change in high volumes of 
fluids are necessary since there is a greater possibility of presenting signs of inflammation. It is also 
limited to the maximum volume to be infused per puncture site, with an average maximum volume 
of 1,500ml / 24 hours per puncture site being cited in the studies, depending on the location of the 
puncture site. It is also worth mentioning the possibility of using two concomitant puncture sites ¹¹, ¹², ¹³, ¹⁴, ¹⁵.

In relation to the competence related to both the puncture and the administration of fluids, 
both people are delegated by the nurse to the nursing technician, provided that the professionals are 
trained, qualified, and qualified for such procedures. A study¹¹ which analyzed the knowledge of 
the nursing team regarding knowledge about a hypodermoclysis found that 100% of respondents 
reported not knowing the nursing care related to this practice, stating that they did not receive any 
guidance from the institution.

Based on these results, the nursing team, along with other health professionals, should build 
and use assistance protocols that will guide the care of patients, thus encouraging the use of the
technique, as well as the investment of clinical research to scientifically support the use of the route in cancer patients.

It can be inferred during the preparation of this analysis, the need for investment in training for the nursing team on the use of the route in the hospital and home environment. Being an inexpensive route, technically easy, less painful, one providing quality of life in patients with uncontrolled symptoms, and it should be applied more frequently in cancer patients.

The studies published on the use of the pathway in cancer patients were found as a limitation of the study, justifying once again the need for not using a time limit in the search for manuscripts.

CONCLUSION

In this research, it was possible to identify hypodermoclysis, its indications, purposes, advantages, and disadvantages, verified in the relative studies of this route of administration of fluids and/or drugs as a possibility of use in cancer patients, especially patients in palliative care.

It was possible to gather and synthesize the knowledge and procedures related to the SC pathway in the patient, having in this review section, the objective of clarifying and encouraging the practice and development of future investigations that can determine the applicability and use of hypodermoclysis, since the lack of published clinical studies on this topic was evidenced in the development of this research, with more investments in analysis on this topic being dealt with.

It can also be demanded that hypodermoclysis is an inexpensive route, easy to apply and that it benefits cancer patients, however, nursing professionals are little known about this route, requiring investment in continuing education with professionals for better dissemination. and use of the technique as a possibility of administering fluids to cancer patients.

It is concluded, then, that a hypodermoclysis is a safe and effective route for use in cancer patients, requiring, however, further studies on the use of the route as treatment therapy and symptom control of cancer patients, as well as in patients in palliative care, with this foundation we will be able to qualify and provide comfort assistance to the patient and his family.

CONTRIBUTIONS

It should be noted that all authors contributed equally in the design of the research, collection, analysis and discussion of data, as well as the writing and critical review of the content with intellectual contribution and in the approval of the final version of the study.

CONFLICTS OF INTERESTS

There was no conflict of interest in the construction of the manuscript.
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