



## Complications of the subcutaneous route in the infusion of medications and solutions in palliative care

Complicações da via subcutânea na infusão de medicamentos e soluções em cuidados paliativos

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**Objective:** to characterize the complications associated with the use of the subcutaneous route for infusion of drugs and solutions in palliative care. **Methods:** observational, prospective study conducted at the Palliative Care Unit of a general teaching hospital. **Results:** the study analyzed seventy-eight patients in palliative care, in whom 254 punctures for infusion of drugs and/or solutions through the subcutaneous route were made. Most patients were elderly (87.3%) and malnourished (69.2%). In 33.0%, the route was indicated for symptom control; in 50.0%, the puncture occurred in the anterolateral thigh flap; 65.4% of the punctures showed no complication. Among the identified complications, 9.4% were edema and 9.1% hyperemia, and 53.8% occurred in the deltoid region. Cellulite occurred in only 3.5%. **Conclusion:** the infusion of solutions using the subcutaneous route can be considered a safe alternative, with risk of complications which are mostly reversible and with low potential to cause damage to patients.

**Descriptors:** Nursing Care; Hypodermoclysis; Palliative Care; Infusions, Subcutaneous.

**Objetivo:** caracterizar as complicações associadas ao uso da via subcutânea na infusão de medicamentos e soluções em cuidados paliativos. **Métodos:** estudo observacional, prospectivo, realizado na Unidade de Cuidados Paliativos de um hospital geral de ensino. **Resultados:** foram avaliados 78 pacientes em cuidados paliativos, nos quais foram realizadas 254 punções na via subcutânea para infusão de medicamentos e/ou soluções. A maioria era idosa (87,3%) e encontrava-se desnutrida (69,2%). Em 33,0%, a via foi indicada para controle de sintomas e, em 50,0%, a punção ocorreu na região anterolateral da coxa; 65,4% das punções não mostraram complicação. Dentre as complicações identificadas, 9,4% foram edema e 9,1% hiperemia, sendo que 53,8% delas ocorreram na região deltoidea. A celulite ocorreu em apenas 3,5%. **Conclusão:** a infusão de soluções pode ser considerada uma alternativa segura, a qual apresenta risco de complicações em sua maioria facilmente reversíveis e com baixo potencial de ocasionar danos aos pacientes.

**Descritores:** Cuidados de Enfermagem; Hipodermóclise; Cuidados Paliativos; Infusões Subcutâneas.

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## Introduction

Population ageing and increased prevalence of cancer and other non-communicable diseases such as hypertension, diabetes mellitus and dementia generated the need to reformulate health care and also to improve techniques that may benefit patients, considering the specificities of this population<sup>(1)</sup>. Once hospitalized, the efforts to care for patients usually return to interventions aimed at cure, which often requires the use of invasive methods, not always resulting in benefits. Such approaches do not frequently match the needs and possibilities of patients and do not take the suffering they cause into account<sup>(2)</sup>.

Given this context, the offer of palliative care has gained gradually more support, particularly the therapies for the patient's needs presented according to the natural evolution of the disease. The concept of palliative care was defined by the World Health Organization in 1990 and directed only to cancer patients aiming at end-of-life care. In 2002, the concept was revised and expanded to patients with other chronic and degenerative diseases. In 2004, the World Health Organization considered palliative care measures as those capable of improving the quality of life of patients and their relatives in the face of life-threatening diseases that through prevention and relief of suffering, disclosing a new document. This new approach extended the horizons of action of palliative care, not restricting it to protocols, but extending it to the individuality of the contexts of these patients and their families<sup>(3)</sup>.

In the modality of palliative care, the oral route is chosen for drug administration because it is the simplest and the less invasive. In cases where the oral route is not feasible because of possible damage to the patient, other routes can be considered. Up to 70.0% of patients who face life-threatening diseases eventually need an alternative route for drug administration, usually due to lower level of consciousness and inability to swallow<sup>(4)</sup>. In such cases, the subcutaneous route is an option for administering medications and

fluids when the oral route is contraindicated, such as in patients suffering from dysphagia, persistent nausea and vomiting, constipation and diarrhoea, for it allows to address dehydration cases that do not require quick volume restitution<sup>(5)</sup>. Patients with mental confusion and severe dyspnea can also benefit from the use of the subcutaneous route<sup>(4)</sup>.

The subcutaneous route is considered more comfortable and less painful for patients when compared to venous puncture, and the easy insertion decreases the number of unsuccessful puncture attempts. Although care management of the subcutaneous route is a safe practice, it is not risk-free. A recent integrative review found that among the main adverse effects related to the use of hypodermoclysis (infusion of solutions in the subcutaneous tissue) are pain and edema, cellulitis and insufficient absorption of the solution with accumulation of liquid at the puncture site<sup>(6)</sup>. These risks are considered simple because they do not bring major harm to the patients, but they will only be minimized or avoided if they are known and problematized in the care, teaching and research spheres, considering that the guiding framework of the caring process in palliative care focuses on the welfare and relief of patients' suffering.

Despite its advantages, such as the greater ease of puncture and lower risk of serious complications<sup>(7)</sup>, the use of the subcutaneous route for infusion of drugs and solutions is still considered an underutilized practice in the care clinic. Thus, studies on this procedure are needed, which was the motivation of the development of the present study. The questions that guided the investigation were: what are the main indications, puncture sites, and length of permanence of the device in the subcutaneous route? Are there any factors that may influence the occurrence of complications when using this route?

In this context, this study aimed to characterize the complications associated with the use of the subcutaneous route for infusion of drugs and solutions in palliative care. The study contributes to advances in knowledge about the use of the subcutaneous route

in patients who are in palliative care and, therefore, to expand this practice in a safe and effective way among patients, professionals and health services.

## Methods

This is an observational, prospective study where all patients hospitalized and using the subcutaneous route for infusion of drugs and solutions in a palliative care unit were followed up over four months (May to August 2018). The inclusion criteria were patients older than 18 years, hospitalized in the palliative care unit and using the subcutaneous route for infusion of drugs and solutions. We excluded procedures done before hospitalization in the palliative care unit.

The study was conducted in a large, public teaching hospital providing general care. The institution has an exclusive unit dedicated to palliative care, with 16 beds. In 2018, the hospital received an average of 50 patients per month from Belo Horizonte and the metropolitan region. The nursing resident researcher who was present at the service from Monday to Friday collected the data. On weekends, nurses on duty were instructed to make the necessary records and assist the patients. It is noteworthy that all nurses working in the unit were trained by the institution on care and use of the subcutaneous route and were able to identify the presence of complications.

Sociodemographic and clinical data were collected from medical records to characterize the study population, including sex, age, and nutritional status, diagnosis of poor prognosis and outcome of the patients monitored. In the modality of palliative care, the defining diagnosis of poor prognosis adopted considers the possibility of indication for those patients with terminally ill conditions, with important pain and/or suffering<sup>(8-9)</sup>.

Patients using hypodermoclysis and who met the eligibility criteria were evaluated on a daily basis, once a day, and information on the puncture was recorded in a data collection instrument prepared by

the authors, adapted from a form used by the Hospice of the Clinical Hospital of São Paulo-Jaçanã for evaluation of hypodermoclysis. The patients were followed up until they were discharged, died or stopped using the subcutaneous route for administration of drugs and solutions.

Data about the procedure were collected during daily observation, including the indication of the use of the route; puncture site; drugs infused in the route; length of permanence of the device; device used in the puncture; type of clamping device used. The type of complication (hyperemia, edema, cellulitis, bleeding, pain, abscess, and necrosis) and site of occurrence were used to classify the occurrence of complications. Some data were retrieved from electronic medical records, the patients themselves, or their relatives present in the room.

Statistical analyses included frequency distribution and descriptive measures using the Statistical Package for the Social Sciences, version 23. Stratified analyses were also made to check for possible correlations between the variables. In the descriptive analyses, each patient was counted only once (n=78). As for the punctures, each one was analyzed independently, and thus, the same patient could generate more than one puncture record (n=254). In the analysis of punctures, dependence/influence between punctures in the same patient were not considered. In the correlations analysis, it was investigated whether the relationship between two or more variables was statistically significant, adopting the significance level of 95%. Situations in which the values did not reach 95% were not presented.

The study was approved by the Ethics and Research Committee of the Federal University of Minas Gerais under Opinion nº 2,745,989/2018.

## Results

Seventy-eight patients who had 254 punctures in the subcutaneous route for infusion of drugs and solutions during the study period were followed up. Of

these, 42 (53.8%) were women and 36 (46.2%) men. The mean age was 78 years with a standard deviation of 13.5. The majority of the patients, 38 (48.7%), were between 60 and 79 years old; 30 (38.6%) were older than 80 years; and 10 (12.8%) were between 40 and 59 years old. The diagnosis of nutritional status was collected from medical records, and 54 (69.2%) patients were considered malnourished, 14 (17.9%) eutrophic, 6 (7.7%) obese, and 4 (5.1%) had no information of nutritional status in the medical records.

In the researched population, the prevalent definers of poor prognosis were advanced dementia, 25 (32%), followed by oncologic disease, 17 (21.7%), frailty, 17 (21.7%), neurological disease, 12 (15.3%), organ failure, 4 (5.1%), and others, 3 (3.8%). Most of the study participants, 73 (93.6%), were in the end stage of the disease. Regarding the outcome of the patients, 41 (52.6%) died, 31 (41.0%) were discharged from the hospital, and 5 (6.4%) transferred to another institution.

Regarding the indication for the use of the subcutaneous route, this was used to control symptoms in 84 situations (33.0%), due to difficult access to the peripheral venous system in 66 (25.9%), for the purpose of hydration in 47 (18.5%) and for other purposes in 29 (11.4%), as in situations in which the infused medication required exclusive route.

Among the 254 punctures for the subcutaneous access route, 127 (50.0%) were made in the anterolateral thigh flap, 61 (24.0%) in the abdominal region, 52 (20.5%) in the deltoid region, 11 (4.3%) in the infraclavicular region, and 3 (1.2%) in the interscapular region. In all cases, the device chosen was a needleless catheter number 22 or 24. In 250 (98.4%) punctures, the device was fixed with sterile transparent film and in 4 (1.5%) punctures with microporous tape. The length of stay of each device ranged from less than 24h to six days, with an average of 3.5 days.

The main reason for removal or replacement of the device in the subcutaneous route, 89 (35%), was the fact that the standard time for exchange adopted in the institution was reached, which was five days. Exchanges due to complications occurred in 41 (16.1%)

situations. Other causes for removal of the device from the subcutaneous route were: death of the patient, 44 (17.3%); loose fixation during manipulation of the device, 21 (8.3%); removal of the device by the patient, 21 (8.3%); discharge of the patient, 18 (7.1%); removal of the device according to medical prescription, 13 (5.1%); and no record of the reason for withdrawal of the device, 7 (2.8%).

As for the solutions and drugs administered in the subcutaneous route, serum (sodium chloride 0.9%) was administered in 155 (61.0%) situations, with caloric intake or in combination with other medications. The most infused drug was morphine, prescribed in 124 procedures (48.8%), followed by dipyrone in 82 procedures (32.3%) and scopolamine in 58 procedures (22.8%). The other medications infused and that appeared in less than 20.0% of the procedures were: haldol (16.5%); metoclopramide (15.7%); ondansetron (9.8%); ceftriaxone and meropenem (9.4% each); omeprazole (8.7%); furosemide (8.3%); dexamethasone (7.1%); ranitidine (5.9%); midazolam (5.1%); teicoplanin (4.3%); phenobarbital (3.9%); cefepime (3.1%); tramadol (1.6%); methadone (1.2%); and ampicillin (0.8%).

Complications were absent in the majority (65.4%) of the 254 punctures performed. In the 34.6% cases in which complications happened, edema (9.4%) and hyperemia (9.1%) prevailed. Regarding the relation between the occurrence of complications and puncture site, it was found that punctures in the deltoid region presented more complications. Of the 52 punctures performed, 28 (53.8%) presented some kind of complication.

The occurrence of complications in the other regions had the following incidence: 40 complications (31.5%) in the 127 punctures performed in the anterolateral thigh flap; 19 complications (31.1%) in the 61 punctures performed in the abdomen and; 1 complication (9.1%) in the 11 punctures performed in the subclavicular region; and no complications were identified in the in the three punctures performed in the interscapular region.

Table 1 describes the complications observed

in each puncture site, with edema prevailing in the deltoid region (35.7%), followed by hyperemia in the thigh region (32.5%). The occurrence of cellulitis was higher in the thigh region (12.5%).

**Table 1** – Type of complication by puncture site

Site	Edema (%)	Hyper-emia (%)	Pain (%)	Cellulitis (%)	Bleeding (%)	Hemato-ma (%)	Others (%)
Deltoid region	35,7	14,2	17,8	7,1	-	-	25,0
Thigh	22,5	32,5	10,0	12,5	2,5	2,5	17,5
Abdomen	26,3	31,5	15,7	10,5	-	-	15,7

Table 2 shows the main drugs infused in punctures in which complications were identified. A higher prevalence of complications associated with the use of ranitidine and metoclopramide was observed.

**Table 2** – Complications related to drugs infused through the subcutaneous route

Drug	Hyper-emia (%)	Bleed-ing (%)	Celluli-tis (%)	Pain (%)	Edema (%)	Punctions (%)	Complica-tions (%)
Ranitidine	40,0	6,6	20,0			15	53,3
Cefepime	-	-	-	25,0	37,5	8	37,5
Teicoplanin	18,1	-	-	-	-	11	36,3
Metoclopra-mide	22,5	-	15,0	15,0	17,5	40	30,0
Ceftriaxone	12,5	-	-	4,1	16,6	24	25,0
Meropenem	12,5	-	-	4,1	4,1	24	25,0
Dipyron	14,6	1,2	6,1	8,5	14,6	82	24,3

## Discussion

The study as limitations the impossibility of calculating predictive measures that favor better care practices, as well as determining the causality of complications arising from the use of the subcutaneous route for infusion of drugs and solutions in palliative care patients. However, the study provides findings that contribute to the elucidation of the use of this therapeutic modality.

The study participants, most malnourished elderly people, had a worrying social and clinical profile that favors the occurrence of complications of their general health status. Among them, 21.7% had neoplasia, also observed in other studies conducted with patients in palliative care. The indication of this therapeutic modality for oncological patients is frequent and consistent due to the fact that cancer affects biopsychosocial aspects of the person and his/her family, especially when the disease is in an advanced stage and with metastases, with low therapeutic possibility of cure<sup>(10-12)</sup>.

However, in patients with other diagnoses, such as neurological disorders, present in most study participants, palliative care is necessary to promote global well-being. In cases of advanced dementia, the interventions foreseen in palliative care are also important when there are evidences of structural alterations and functional impairments<sup>(8,13)</sup>.

Frailty proved to be the main definer of poor prognosis. The literature indicates that elderly people in conditions of severe frailty, even without specific diagnosis, who show a progressive decline of vitality and appear to develop a predictable trajectory toward death within the following months can also be indicated for palliative care in order to improve their quality of life<sup>(8,14)</sup>.

The percentage of deaths was lower than in other palliative care services, which is usually higher than 70.0%<sup>(10)</sup>. We believe that the percentage of patients with hospital discharge as outcome, despite their clinical condition in which complex health problems and frailty predominated, was a result of effective control of symptoms, thus pointing out the quality and effectiveness of the palliative care provided to this population.

Regarding the indication of the subcutaneous route, the results obtained corroborate with a study conducted with 16 patients in palliative care in which the this route was indicated for control of symptoms such as dysphagia, nausea and vomiting, agitation and prostration<sup>(15)</sup>. This route has also been widely used

for hydration, considering the high risk of dehydration in the population with this clinical profile<sup>(4)</sup>.

On the perspective of hydration, an English study<sup>(16)</sup> pointed out that the subcutaneous route provides a series of advantages over the intravenous route for individuals who do not tolerate enteric fluids and need hydration, because the former is associated with less complications as well as a wider variety of infusion sites. This makes it particularly advantageous for frail and/or elderly patients who need low-volume hydration for safe administration of fluids, even in the home environment.

With regard to puncture sites, the literature indicates the subclavicular region, interscapular region, abdominal region (flanks), anterolateral thigh flap, and deltoid region as the most indicated<sup>(4)</sup>, in line with the findings of the present study. The high percentage of punctures in the anterolateral thigh region stems from the poor nutritional status of the majority of the assisted patients.

The abovementioned regions present a thicker subcutaneous tissue layer, with greater capacity to receive large volumes, stressing that hydration is an important indication for the use of the route. It is noteworthy that in the choice of the puncture site it is necessary to take into consideration the volume of liquid to be administered; the abdominal and anterolateral regions of the thigh are good options in these situations<sup>(4)</sup>, and hydration was one of the predominant indications for the use of the route.

The choice for the use of needless catheters is justified by their flexibility and lower risk of skin trauma to the patient, as well as a lower risk of occupational accidents for the profession<sup>(15)</sup>. As for fixation, sterile transparent film is recommended in the institution and is in accordance with the most recent recommendations<sup>(4)</sup>. This material not only protects and avoids the occurrence of infections at the puncture site, but also allows the visualization of the puncture site all the time. In addition, it contributes to preventing the loosening of the device.

As for the average length of permanence of

the device, the institutional protocol recommends to change the device every 5 days. The extension of the recommended deadline may occur in atypical situations, as assessed by the nursing team. There is no consensus in the literature about the maximum time. The recommendation is that, when any complication appears, the device must be removed no matter how recently it was installed and a new puncture must be performed at a minimum distance of five centimeters from the initial site<sup>(4)</sup>. Removals due to complications corresponded to the minority of the situations, giving evidence of the safety of the use of this resource in health treatment.

Regarding the complications in the use of the subcutaneous route for infusion of drugs and solutions, edema and hyperemia prevailed. These are characterized by being of low severity, reversible and with little clinical repercussion for the patient, requiring only the reduction of the infusion rate or the creation of a new puncture site<sup>(6)</sup>, a conduct adopted in the institution. Cellulitis was the most severe complication, but it occurred in a very small number of situations (3.5%). This complication requires the use of antibiotics, cold compresses and daily monitoring of the affected site<sup>(4)</sup>.

Punctures done in the deltoid region were the ones in which more complications occurred, being manifested in the form of edema. It is believed this happens due to the smaller amount of subcutaneous tissue when compared to the abdominal region and anterolateral thigh flaps. Thus, the deltoid region should be avoided for continuous infusion of solutions such as serotherapy, or should be used only when puncture is not possible in other sites with greater amount of subcutaneous tissue<sup>(4)</sup>.

Serum (sodium chloride 0.9%) with or without caloric intake or in combination with other medications and morphine predominated among the administered fluids, which corroborates with findings of other studies<sup>(15,17)</sup>. Other infused medications are described in other studies with people in palliative care. One of them pointed out that the drugs most infused

by this route were morphine, scopolamine, metoclopramide, cefepime, ondansetron, sodium chloride 0.9%, dipyrone, haloperidol, chlorpromazine, dexamethasone and furosemide<sup>(17)</sup>.

However, the findings do not allow conclusions regarding the occurrence of complications in relation to medications used by patients, and further studies are necessary. It is worth noting that the best tolerated solutions are isotonic, water soluble, and those with pH close to neutrality because they cause fewer irritant reactions<sup>(4,16-18)</sup>.

The present results indicate that the use of the subcutaneous route for infusion of drugs and solutions is a viable and effective alternative, which could be used in situations other than palliative treatment, and the nursing team should be responsible for the procedure. It is up to the entire multiprofessional team to analyze the different situations in which this route can be used, as well as the results achieved, considering the complications and interactions, in order to avoid them, offering a care that considers the particular conditions of the patients in an individualized and comprehensive approach<sup>(19-20)</sup>.

## Conclusion

The results found in this study indicate that the use of the subcutaneous route for infusion of drugs and solutions can be a safe alternative whose risk of complications is reversible and present low potential to cause damage to patients in the majority of cases. The nursing team needs continuous training to reduce the occurrence of complications, even if mild. Further studies to contribute to deeper analyses of the causality of the complications occurring during the use of the subcutaneous route are recommended.

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## Collaborations

Guedes NAB collaborated with the drafting, design, analysis and interpretation of the data, writing of the article and relevant critical review of the intellectual content. Melo LS, Santos FBO and Barbosa JAG collaborated with the drafting of the article, relevant critical review of the intellectual content and final approval of the version to be published.

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