Impact of compounded drugs on the caregivers' burden of home therapy management in pediatric palliative care: A descriptive study

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Abstract

Background: Children with medical complexity need complex assistance, that considerably affects caregivers' quality of life. They often need multiple medications, with a consequent relevant risk of errors or poor compliance. Galenic (or compounded) drugs are blended in the pharmacy's laboratory worldwide according to different rules and tailoring the patient's needs. While their use may sometimes simplify these therapies, little is known about parents' attitude about this issue.

Aim: This study aimed at investigating the complexity of the daily therapy management and exploring the parents' opinions about galenic compounds.

Design: Parents were interviewed by using a structured questionnaire.

Setting: Children followed by the Pediatric Palliative Care Network in Friuli Venezia Giulia, Italy, were included from November 2021 to April 2022. Those diagnosed with malignancies were excluded, since therapies are mainly administered through a central venous catheter.

Results: Thirty-four parents were interviewed. Fourteen patients took drugs orally, one via nasogastric tube (NGT), 18 via gastrostomy, and one orally + NGT. The mean number of drugs taken every day was six (2–14), in mean 10 (3–18) administrations, that overall required a mean of 44 (8–180) minutes to be delivered. Twenty-eight parents used galenic compounds, and 24 reported relevant advantages, because of a ready-to-use and safe formulation.

Conclusions: The therapy management of children with medical complexity relies on parents. Galenic compounds may improve both patients' and caregivers' quality of life, either in terms of shorter time of administration or smaller risk of errors. Therefore, their use should be encouraged worldwide, according to the different reference rules.

Keywords

Caregivers, children, drugs, therapy

What is already known about the topic?

- The burden of treatments' administration for children with medical complexity fell mainly on parents.
- Many common drugs do not adequately fit with feeding devices (e.g., percutaneous endoscopic gastrostomy, nasogastric tube).
- Children with medical complexity are often treated with off-label drugs.

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What this paper adds:

- The home therapy management of children with medical complexity consistently impacts on the caregivers' quality of life.
- The home therapy management is time-consuming, with a consequent high risk of either errors or poor compliance.
- Compounded drugs may overcome many problems often faced during the home therapy management and may improve either the children's or caregivers' quality of life.

Implications for practice, theory, or policy:

- The use of compounded drugs may help caregivers in the daily home therapy management, by reducing either the time of administration or the risk of errors or poor treatment adherence.
- The use of compounded drugs in pediatric palliative care should be encouraged and promoted.

Background

Children with Medical Complexity constantly require complex assistance either in terms of drug administration or daily personal care. Living at home increases their families' care responsibilities,[1] and this inevitably falls on the relatives' well-being and quality of life, in particular on parents and siblings.[2,3]

Caregivers are mainly parents, even though sometimes also relatives, nurses, or caretakers contribute to these children's care. One of the main caregivers' (parents, relatives, nurses, etc.) daily task is the therapy administration. These children often need many medications every day, and this may further affect their caregivers' quality of life. Furthermore, children with medical complexity are often fed by percutaneous endoscopic gastrostomy (PEG) or nasogastric tube (NGT), and it frequently happens that drug formulations on the market do not adequately fit with these systems. For example, this is the case of lansoprazole, whose orodispersible capsules must be ground and dissolved, and then pushed through the tube. Nonetheless, microgranules cannot be completely dissolved and it frequently happens that their aggregation obstructs the feeding device. Moreover, when left too long diluted in the syringe, it takes a purple color and, day after day, the PEG's tube or button and the NGT become inevitably violet. Another example is the ciprofloxacin syrup, possibly used for *pseudomonas* colonization treatment, whose formulation available on the market is dense and grainy, which is extremely difficult to be pushed through the tube. Remarkably, in this setting these drugs are not being used as prescribed, but rather with an unlicensed use in most jurisdictions, with responsibility transferred from manufacturer to prescriber and those administering the drugs. Moreover, these children's clinical complexity is not always manageable with the on-label medications, and drugs are prescribed in different conditions than those for which they had been authorized, in terms of age, route of administrations, indication, dosage, or formulation.[4,5] Furthermore, caregivers must often manipulate drugs before the administration, such as grinding the capsules and/or melting the powder to make them suitable for the feeding device, and this takes a lot of time every day. This may further increase the risk of either errors in the dose or timing of administration or in the compliance and treatment adherence. For these reasons, off-label drugs are often used to face these problems.[5–7]

The use of galenic compounds has already been reported[8–10] to be an effective tool to simplify these patient's therapy, either in terms of type of formulation or time of delivery. Galenic (or compounded) drugs are accurately blended in the pharmacy's laboratory following accurate preparation laid down in the official pharmacopeia, so as to be as safe and effective as the industrial product. Remarkably, galenic preparations can be prepared tailoring each specific patient's needs: the formulation and the drug concentration can be chosen according to the patient's feeding device and body weight. Moreover, galenic drugs are prepared under a medical prescription which precisely define the dosage and the duration of the therapy. Therefore, either the pharmacist or doctors may indirectly verify whether the compliance is good: either an early or delayed request of more drugs from parents may be a sign of errors in the administration. Furthermore, another important value of galenic preparations which has been recently pointed out is their prompt availability in case of short supplies of the market.[11] Galenic drugs are used worldwide according to different national rules, which regulate their production and certify their safety and effectiveness. Drugs' formulations are described in the monographs of the drugs included in the pharmacopeia, so in each country these drugs may be prepared according to the reference regulations.[12]

The aims of this study were to investigate the complexity of the daily therapy management routine and to explore the parents' knowledge and opinions about the use of galenic compounds and their effectiveness in simplifying the caregivers' tasks.

Methods

Study design and setting

This is a descriptive study with families with children with medical complexity eligible to Pediatric Palliative Care, followed by Regional Pediatric Palliative Care Network in Friuli Venezia Giulia, Italy, in three main pediatric hospitals in three cities of the region (Trieste, Udine, and Pordenone).

No validated questionnaires are available in the literature with the aim of investigating the complexity of the home therapy management in pediatric palliative care. Therefore, we created an *ad hoc* questionnaire underpinned by a careful literature analysis on the topic. At first, we investigated which were the main aspects and difficulties of the home therapy management of children with medical complexity, by looking for previous studies which had focused on these issues. Then, we created a first draft of the questionnaire which we would like to administer to parents, with questions investigating these main issues. They were asked for their daily therapy administration routine, its complexity, the impact on their quality of life, and the use of any galenic compounds. At first, we administered the questionnaire to five parents, then we modified it according to the issues that had been found. Then, once the questionnaire was completed (Supplemental material n.1), we administered it to all parents.

Study population and recruitment

The population under study were families with pediatric patients diagnosed with chronic and incurable diseases eligible to Pediatric Palliative Care, followed by the Regional Pediatric Palliative Care Network in Friuli Venezia Giulia, Italy. Those children diagnosed with malignancies were excluded because they usually have a central venous catheter by which the main therapies are administered, and because, when eligible for specialist palliative cares, they are mainly at the end of life, thus representing a particular population not covered by this study.

According to these criteria, we selected families followed by the Network from November 2021 to April 2022. We asked them whether they would like to participate to this study, and then we interviewed those who had accepted.

Data collection and analysis

Parents were interviewed by pediatricians or a nurse (FB, VT, EP, and MT), and data were collected in a personal database.

Data were analyzed using descriptive statistics. Continuous and discrete variables were expressed as absolute frequencies.

Ethical issues

The study was approved by the ethical committee N° 315/2020.

Informed written consent for data publication was obtained by all caregivers.

Results

i) Patients background

Sixty-three families were followed by the Regional Network. Eighteen were excluded because children were affected by malignancies. Eleven parents refused to take part in this study. Finally, thirty-four caregivers were interviewed.

Children were followed by the three main Pediatric Hospitals of Friuli Venezia Giulia: Trieste (18, 53%), Udine (8, 23.5%), and Pordenone (8, 23.5%). Children were 23 (67.6%) male and 11 (32.4%) female.

The mean age was 8.5 years (range 0.7–19, median 7.5, interquartile range (IQR) 8). Ten (29.4%) patients were under 5 years old, 10 (29.4%) from 5 to 10, while 14 (41.2%) were 10 years old or older. Children were affected by neonatal asphyxia (8, 23.5%), genetic (16, 47.1%), congenital (1, 2.9%) or acquired (4, 11.8%) conditions, or unknown diseases (5, 14.7%), all eligible to specialist pediatric palliative care.

ii) Type of medications and route of administration

Fourteen (41.2%) children took medications orally, one (2.9%) via NGT, 18 (53.0%) via PEG, and one (2.9%) both orally and via NGT. On average, every day these patients took 6.4 drugs (range 2–14, median 6, IQR 4), in 10 different administrations (range 3–18, median 9.5, IQR 7.7), that overall required at least 47 (8–180) minutes (median 30, IQR 59) to be prepared and administered. The main patients' characteristics are listed in Table 1. Medications were mainly antiepileptics (31.8%), proton pump inhibitors (10.9%), and benzodiazepines (6.4%). All drug categories are shown in Table 2. Table 3 shows the number of drugs needed every day and the route of administration in relation to the type of disease.

Twenty-nine (85.3%) caregivers have to manipulate drugs before the administration (e.g., grinding, melting), so as to make them suitable for the feeding device. On average, they must open the NGT or the PEG four times a day, besides the normal nutrition (range, 0–34, median 2.5, IQR 6).

Table 1. Patients' characteristics.

	N (%)	Range
Total	34	
Male	23 (67.6)	
Female	11 (32.4)	
Age (years)		
<5	10 (29.4)	
5–10	10 (29.4)	
⩾10	14 (41.2)	
Median	7.5	0.7–19 (IQR 8)
Disease		
Neonatal asphyxia	8 (23.5)	
Genetic condition	16 (47.1)	
Congenital condition	1 (2.9)	
Acquired condition	4 (11.8)	
Unknown	5 (13.7)	
Administration route		
Orally	14 (41.2)	
NGT	1 (2.9)	
PEG	18 (53.0)	
NGT + PEG	1 (2.9)	
Total daily medications (median)	6	2–14 (IQR 4)
Total daily administrations (median)	9.5	3–18 (IQR 7.7)
Total daily time of preparation/ administration (median, min)	30	8–180 (IQR 59)

NGT: nasogastric tube; PEG: percutaneous endoscopic gastrostomy.

Table 2. Drugs categories.

	N	%
Antiepileptics	70	31.8
Proton pump inhibitors	24	10.9
Benzodiazepines	14	6.4
Vitamin D	14	6.4
Anticholinergics	13	5.9
Laxatives	10	4.5
Antispastics	9	4.0
Adjuvants	7	3.2
Topic agents*	7	3.2
Antihypertensives (ACE-inhibitors, sartans)	6	2.7
Sleep medications	6	2.7
Antibiotics (prophylaxis)	5	2.3
Immunosuppressors	2	0.9
Other vitamins, iron supplementation	2	0.9
Prokinetics	2	0.9
Antipsychotics	2	0.9
Beta-blockers	1	0.5
Aspirin	1	0.5
Other**	25	11.4
Total	220	

*Eye drops (e.g., timolol), nebulizer treatments (e.g., ipratropium bromide, antibiotics).
**For example subcutaneous immunoglobulins, heparin, levothyroxine, erythropoietin, ursodeoxycholic acid.

iii) Caregivers' tasks for the home therapy management

Two (5.9%) caregivers prepared the whole daily therapy once a day in the morning, while the rest of them did it before each administration. Therapies were mainly prepared by both parents (16, 47.1%) or mothers (15, 44.1%), while just a few by fathers (3, 8.8%) or other caregivers such as grandparents (2, 5.9%), nurses (1, 2.9%), or caretakers (1, 2.9%). The same trend was reported for the therapy administration: therapies were mainly delivered by both parents (16, 47.1%) or mothers (15, 44.1%), and less frequently by fathers (3, 8.8%), grandparents (2, 5.9%), aunts (1, 2,9%), nurses (1, 2.9%), or caretakers (1, 2.9%).

Eleven (32,4%) caregivers admitted they had to set alarms to remind each administration, also because the last one often takes place late at night (e.g., 11.30 p.m.) or early in the morning (e.g. 6.00 a.m.). All parents used a personal sheet to schedule the therapy (Figure 1). Fifteen caregivers (44.1%) reported that the management of therapy did negatively impact on their quality of life, while 19 (55.9%) considered it as part of their daily routine.

iv) Difficulties in the therapy management and galenic compounds experience

Caregivers reported that they had had doubts (13, 38.2%) or problems (19, 55.9%) while preparing or delivering therapies. They reported difficulties in pushing the medication through the NGT or the PEG's tube and cases of obstruction of the tube. Nonetheless, they often managed to solve these problems by themselves or by contacting the reference hospital or pediatrician.

Twenty-eight (82%) patients had previously been treated or were still being treated with galenic compounds at the time of the interview. Three of them had been treated with galenic compound in the past, while 25 were still under treatment. Among all these patients, 14 (50%) were affected by genetic conditions, five (17.9%) by neonatal asphyxia, five (17.9%) by unknown diseases, and four by acquired conditions.

Among those children who were still being treated with galenic drugs, these compounds represented from the 8.3% to the 57.1% of all drugs administered every day. Galenic compounds were mainly proton pump inhibitors syrup (22/25, 88%), glycopyrrolate syrup (9/25, 36%), and baclofen syrup (9/25, 36%), less frequently antibiotics (azithromycin syrup 2/25, 8%), anticonvulsants (cannabidiol syrup, 2/25, 8%; vigabatrin syrup, 1/25, 4%; phenobarbital syrup, 1/25, 4%), ursodeoxycholic acid syrup (2/28, 8%), and beta-blockers syrup (carvedilol syrup, 1/25, 4%).

Twenty-four (70,6%) caregivers reported that the switch from the commercial to the compound formulation had consistently improved the therapy management mainly because of the ready to use and easy to administer

Table 3. Number of daily drugs and route of administration in relation to the type of disease.

Type of disease (*n*. patients)	Number of drugs (daily)		Route of administration			
	Mean/median	Range	Oral	NGT	PEG	Oral + NGT
Genetic condition (16)	6.6/6	3–12	7	–	8	1
Neonatal asphyxia (8)	5.1/5.5	2–8	3	–	5	–
Acquired condition (4)	6.3/6.5	3–9	1	1	2	–
Congenital condition (1)	–	–	1	–	–	–
Unknown (5)	9/10	3–14	2	–	3	–

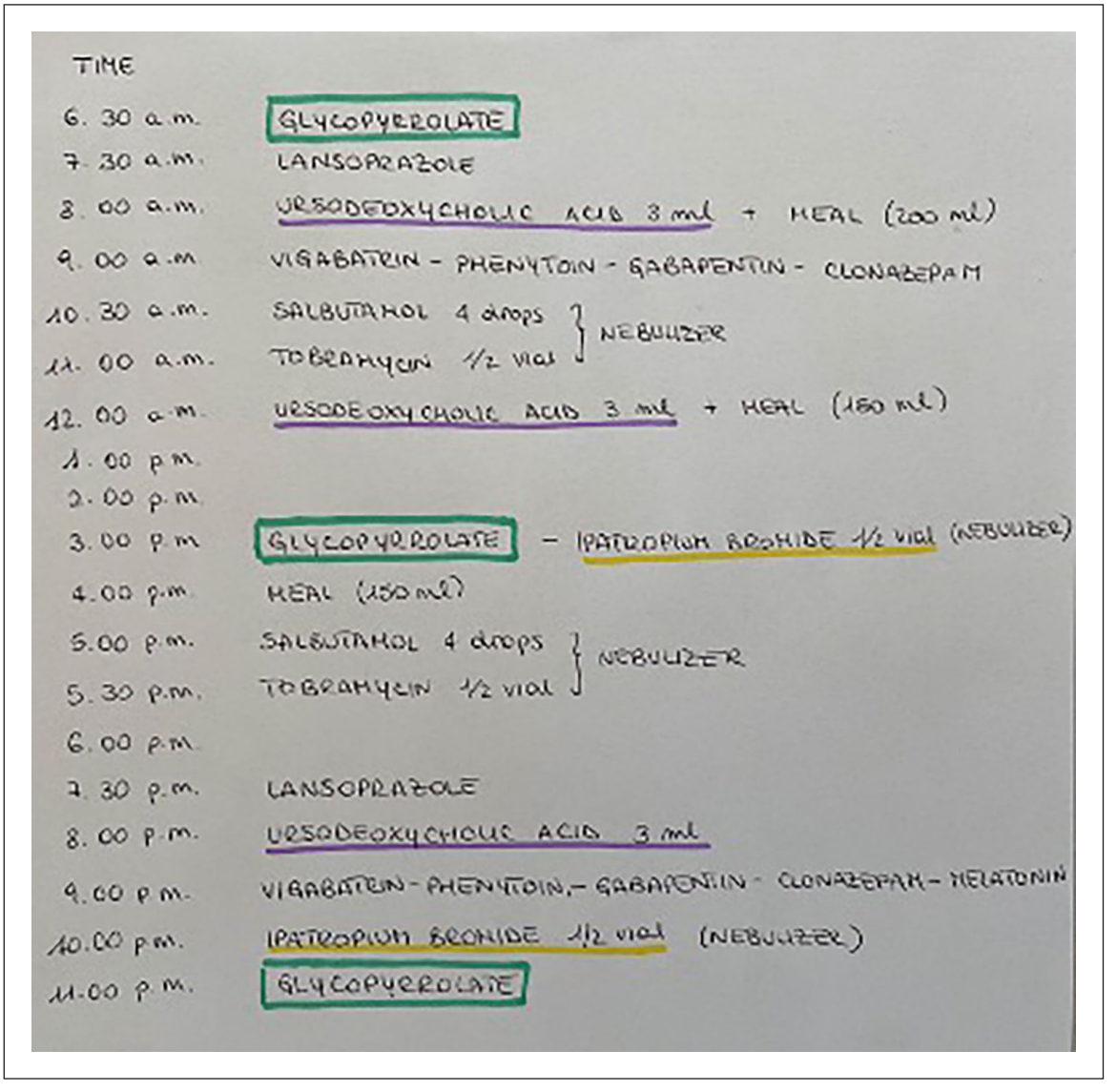

Figure 1. An example of personal sheet created by caregivers to schedule the daily therapy administration.

formulations. However, in two (5.9%) cases the use of galenic compounds was reported as further complication due to the need of fridge storage and limited portability when compared to the commercial product. Two (5.9%) caregivers did not report any advantage neither disadvantage in the use of galenic formulations. Galenic compounds were mainly delivered by the hospital pharmacy through the health district, less frequently by private pharmacy or by the hospital pharmacy or the health district by themselves.

Discussion

i) Main findings of the study

This study highlighted how the home therapy management of children with medical complexity eligible to pediatric palliative care consistently impacts on their caregivers' quality of life. The burden of treatments' administration fell mainly on parents, with a rare involvement of other caregivers. This reflects what has been already reported by other authors: parents mainly manage their children alone.[2,13]

The first issue highlighted in this study is how the caregivers' daily routine is punctuated by the timing of the different therapies. The need of multiple administrations characterized all patients, who took two or more different drugs every day.[14] Many caregivers had to schedule their day according to their children's needs and they often had to set alarms as a reminder for each task.

The second relevant issue is the large amount of time spent every day to prepare and administer therapies and the frequent need to manipulate drugs, with a consequent further expenditure of time and a risk of either errors or hitches with the feeding devices.

Finally, this study reported that galenic compounds consistently improved the daily home therapy management of children with medical complexity mainly because of their easier administration.

ii) What this study adds

In this study the mean daily time required to prepare and administered therapies was about three times greater than what already reported.[2] This could be due to the different characteristics and medical needs of the patients involved in the studies; therefore, it is difficult to compare the results. Anyway, it is certain that the daily therapy delivery covers a large part of the whole care needs either in terms of time spent every day or of responsibility and strict necessity of avoiding errors. Nonetheless, the use of many medications and the need of many administrations at different times every day, as well as the need to face the incompatibility between drug formulations and feeding devices, inevitably raises the risk of mistakes or poor treatment adherence. Galenic compounds could fulfill the caregivers' difficulties and simplify the drugs assumption. In fact, they are prepared *ad hoc* according to each patient's needs and characteristics, either in terms of type and flavor of formulations (e.g., syrup, oral suspension) or of dosage. Moreover, galenic preparations may overcome the difficulties in finding effective products on the market[15] or may cut down the costs of their purchase.

The use of galenic compounds and its advantages on pediatric patients has recently been pointed out,[8–10] and this study further confirmed its effectiveness. In fact, the great majority of caregivers who had already used galenic formulations reported a great satisfaction, mainly because of the easiness of administration. It must be considered that some galenic formulations require strict storage conditions and this could be a limit to their use, but the advantages of their use may overcome these limits. Furthermore, galenic formulations are much less expensive than the industrial ones. For example, the costs of a 1 mg of glycopyrrolate are 5.28 € and 0.34 € respectively for the industrial product and the galenic syrup compounded at the hospital pharmacy of the Institute for Maternal and Child Health Burlo Garofolo in Trieste, Italy.[15]

Finally, the introduction of telemedicine and the use of a computerized therapy schedule may help caregivers in administering the right therapy at the right time and reducing the risk of errors. From a broader perspective, the use of telemedicine in pediatric palliative care has recently started to be investigated and its advantages are still scarce.[16,17] Nonetheless, a computerized therapy schedule could minimize the risk of errors and be remotely checked and promptly modified by specialists.

iii) Strengths and limitations of the study

To our knowledge, this is the first study that investigated both the complexity of the children with medical complexity's therapy management at home and the effectiveness of galenic compounds in pediatric palliative care from the caregiver's point of view. The main limits are the small sample and the use of a non-standardized questionnaire to interview the caregivers, but this study could be the base for further ones.

Conclusions

Children eligible to pediatric palliative care require complex assistance that consistently affect their caregiver's quality of life. One of the most important aspects of this assistance is the home therapy management, which is time consuming, with a high risk of errors or poor compliance. Moreover, often drug formulations available on the market do not fit with the feeding devices. Galenic compounds could help caregivers to overcome these difficulties, simplifying the therapy administration and slightly improving the caregivers' quality of life.

Authorship contribution

LDZ and VT conceived the study. FB, VT, EP, MT, and GP collected data. FB wrote the first draft of the manuscript. EB, DZ, and LDZ substantially revised the work. All authors critically revised the manuscript, making substantial contributions and approving the final version.

Data management and sharing

There are no unpublished data.

Declaration of conflicting interests

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Research ethics and patient consent

Research ethics not applicable. Consent for publication was obtained by caregivers.

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Supplemental material

Supplemental material for this article is available online.

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