Original Article

Bundle construction and assessment before antineoplastic extravasation: a methodological study

Construção e avaliação de bundle frente ao extravasamento de antineoplásicos: estudo metodológico

Construcción y evaluación de bundle ante la extravasación de antineoplásicos: estudio metodológico

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Abstract

Objective: To construct and assess the content of a prevention and management bundle regarding the extravasation of antineoplastic agents in adult cancer patients.

Methods: There were three-step methodological study: Scoping Review, bundle construction and expert material assessment. It was developed according to the methodological framework of Pasquali psychometry. It is noteworthy that the bundle was divided into a module with measures to prevent antineoplastic extravasation and another module with conduits before extravasation. For content assessment, the Delphi technique was applied in two rounds (Delphi I [13 judges] and Delphi II [nine judges]) and those items with Content Validation Coefficient (CVC) greater than 0.78 and more than 80.0% consensus. Data were analyzed using descriptive and inferential statistics (Binominal Test).

Results: All bundle requirements reached agreement among judges greater than 80.0%, and all items achieved statistically significant assessment levels. At the end of Delphi II, both bundle modules were expressively valid (prevention of antineoplastic extravasation [CVC=0.93] and ducts before extravasation [CVC=0.96]).

Conclusion: Bundle content has demonstrated high credibility and its adoption in health institutions can contribute to the quality of care and conduct of professionals facing the extravasation of antineoplastic agents in adult cancer patients.

Resumo

Objetivo: Construir e avaliar o conteúdo de um *bundle* de prevenção e condutas frente ao extravasamento de agentes antineoplásicos em pacientes oncológicos adultos.

Métodos: Estudo metodológico, em três etapas: realização de *Scoping Review*, construção do *bundle* e avaliação do material por especialistas. Foi desenvolvido segundo o referencial metodológico da psicometria de Pasquali. Ressalta-se que o *bundle* foi dividido em um módulo com medidas de prevenção do extravasamento de antineoplásicos e outro módulo com condutas frente ao extravasamento. Para avaliação de conteúdo, aplicou-se a técnica de Delphi em duas rodadas (Delphi I [13 juízes] e Delphi II [nove juízes]) e considerou-se válidos aqueles itens com Coeficiente de Validação de Conteúdo (CVC) maior que 0.78 e consenso de mais de 80,0%. Os dados foram analisados através de estatística descritiva e inferencial (Teste binominal).

Resultados: Todos os requisitos do *bundle* alcançaram concordância entre os juízes superior a 80,0%, bem como todos os itens alcançaram níveis de avaliação estatisticamente significativos. Ao final do Delphi II, os dois módulos do *bundle* se apresentaram expressivamente válidos (prevenção do extravasamento de antineoplásicos [CVC = 0,93] e condutas frente ao extravasamento [CVC = 0,96]).

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Conflicts of interest: nothing to declare.

Conclusão: O conteúdo do *bundle* demonstrou alta credibilidade e, sua adoção nas instituições de saúde, pode contribuir para a qualidade da assistência e das condutas dos profissionais frente ao extravasamento de agentes antineoplásicos em pacientes oncológicos adultos.

Resumen

Objetivo: Construir y evaluar el contenido de un *bundle* (conjunto de medidas) de prevención y conductas ante la extravasación de agentes antineoplásicos en pacientes oncológicos adultos.

Métodos: Estudio metodológico, en tres etapas: realización de *Scoping Review*, construcción del *bundle* y evaluación del material por especialistas. Fue desarrollado según la referencia metodológica de la psicometría de Pasquali. Se resalta que el *bundle* fue dividido en un módulo con medidas de prevención de la extravasación de antineoplásicos y otro módulo con conductas ante la extravasación. Para la evaluación del contenido se aplicó el método Delphi en dos rondas (Delphi I, 13 jueces, y Delphi II, 9 jueces) y se consideraron válidos aquellos ítems con Coeficiente de Validez de Contenido (CVC) mayor a 0,78 y consenso de más de 80,0%. Los datos fueron analizados a través de estadística descriptiva e inferencial (Prueba binominal).

Resultados: Todos los requisitos del *bundle* lograron una concordancia superior a 80,0% entre los jueces, así como todos los ítems alcanzaron niveles de evaluación estadísticamente significativos. Al final del Delphi II, los dos módulos del *bundle* demostraron ser significativamente válidos (prevención de la extravasación de antineoplásicos, CVC = 0,93, y conductas ante la extravasación, CVC = 0,96).

Conclusión: El contenido del *bundle* demostró una alta credibilidad y su implementación en instituciones de salud puede contribuir a la calidad de la atención y de las conductas de los profesionales ante la extravasación de agentes antineoplásicos en pacientes oncológicos adultos.

Introduction

Extravasation of antineoplastic agents (AA) is defined as the unintentional instillation or extravasation of these AA into the perivascular space and/or surrounding tissues. It is considered an oncological emergency due to the potential of some drugs to cause harm to the patient. The degree of local damage depends mainly on the toxicity of the respective compound and the amount of drug extravasated.[1,2]

The incidence of extravasation varies greatly. Estimates between 0.01% and 7% are observed in various publications. However, when analyzing the number of adverse events (AE) associated with antineoplastic therapy (AT), the absolute number of extravasations becomes significant. The result can be potentially overwhelming, with long-term implications such as the accuracy of reconstructive surgery and permanent nerve damage, which means that it is more strenuous and debilitating to the patient than its primary disease.[3-5]

Thus, the dermatological toxicity resulting from the extravasation of AT is one of the main AE requiring intensive care by nurses, since it plays a major role in the prevention, identification and follow-up of complications of this AE. Studies indicate that most extravasation can be prevented by the systematic implementation of careful, standardized, evidence-based administration techniques. To minimize the risk of extravasation, nurses involved in cytotoxic drug infusion and management need to be trained in addition to building and implementing preventive bundles and protocols and extravasation management.[4-6,7]

Nursing care includes planning and carrying out interventions to improve people's responses to health problems and life processes. It requires the identification of functional and dysfunctional responses, the proposition of interventions and the assessment of results obtained.[8] The best way to improve processes and optimize the care of patients who are victims of extravasation is to use bundles. Thus, the bundle is a structured way to improve care processes and patient outcomes, i.e., a set of evidence-based practices, when performed collectively and reliably, are proven to improve patient outcomes.[8,9]

In this perspective, the Resolution of the Federal Nursing Council (*Conselho Federal de Enfermagem*), number 569 of 2018,[10] that regulates the performance of nursing professionals in antineoplastic chemotherapy, among specific functions of nurses, is the elaboration of therapeutic protocols in the prevention, treatment and minimization of side effects. Bundles have been widely publicized in hospitals, as when implemented they are effective in preventing and reducing AE.[9,10]

In view of the above, prevention and management of extravasation of AA in adult cancer patients is paramount for the quality of care provided, as it is a serious complication that generates stress in the nursing team and can generate irreversible damage to the patient.[11] There has been a shortage of inter-

national and none national studies in recent years that synthesize the evidence available in the literature, in the context of prevention and management of extravasation of AT.

The relevance of this study is to provide a bundle with the main measures aimed at the prevention and management of extravasation of AA. Thus, it contributes substantially to the provision of quality and harm-free care for the person with malignant neoplasm treated with AT. It is noteworthy that nurses who administer AA need to be aware of the most current evidence for the multiple types of extravasation treatment, as well as the prevention of AT extravasation.

In this logic, this research aimed to build and assess the content of a bundle of prevention and management before the extravasation of AA in adult cancer patients.

Methods

This is a methodological study, based on Pasquali's methodological framework of psychometrics.[12] It was developed in three stages: scoping review, bundle construction and judges/experts' content assessment from May to November 2018.

Initially, the results from the literature review were used to identify scientific evidence on prevention and conduct of nurses regarding the extravasation of antineoplastic chemotherapy in adult patients. It took place through scoping review (according to the recommendations of the international PRISMA-ScR guide[13] and the method proposed by the Joanna Briggs Institute, Reviewers Manual 2017),[14] based on national and international scientific evidence (Annex 1).

The bundle construction stage initially included 64 items, distributed in two modules. The first module focused on prevention measures of antineoplastic extravasation in adult cancer patients. It was subdivided into five modalities: 1) those preventive actions regarding patients, 2) regarding the appropriate device for puncture, 3) regarding the puncture site, 4) regarding the infusion and 5) regarding the nursing staff.

The second module addressed the conducts facing antineoplastic extravasation in adult cancer patients. It was subdivided into three modalities: 1) the general instructions, 2) the specific instructions and 3) how to use the antidotes and compresses. Each modality had its respective items (which were identified by a letter or number in ascending order).

According to evidence-based practice, the studies were analyzed and classified hierarchically according to the proposal of Melnyk and Fineout-Overholt[15]. This proposal organizes the levels of evidence into: level I - derived from systematic review or meta-analysis of randomized controlled trials or clinical guidelines based on systematic reviews of randomized controlled trials; level II - derived from at least one well-designed randomized controlled trial; level III - obtained from well-designed clinical trials without randomization; level IV - from well-designed cohort and case-control studies; level V - originated from systematic review of descriptive and qualitative studies; level VI - derived from a single descriptive or qualitative study; level VII - from the opinion of authorities and/or expert committee reports.[15]

Each of these modules was assessed for the assessment criteria established by Pasquali.[12] These criteria were behavior, objectivity, simplicity, clarity, relevance, accuracy, variety, modality, typicality, credibility, breadth and balance. It is noteworthy that there was a chart clarifying each of these 12 criteria and they were assessed using the Likert scale: "1 - inappropriate (I)", classified as degree of disagreement; "2 - partially adequate (PA)"; "3 - not sure (N)", classified as degree of indecision; "4 - adequate (A)" and "5 - totally adequate (TA)", both as a degree of agreement.

In the bundle assessment stage, in order to reach the number of judges recommended by Pasquali,[12] i.e., six to 20 experts, it was decided to invite a larger number, considering that some might not respond or refuse the invitation.

This process was directed through the analysis of judges selected for the study, intentionally chosen, through the review of curricula in the Lattes Platform (*Plataforma Lattes*) of the Brazilian National Council for Scientific and Technological

Development (CNPq - *Conselho Nacional de Desenvolvimento Científico e Tecnológico*). For this, we used the simple search form, in the field "search for", in the category "subject", using the terms "oncology" and/or "chemotherapy". Three hundred and twenty-five doctors were identified.

For the screening of possible judges, Fehring's model[16] was adapted and used, since it gives a maximum score of 14 points, however, for this selection was assigned a minimum score of five points, namely: master's and doctorate in nursing or related areas (mandatory criteria), dissertation addressing cancer care (2 points), oncology thesis (2 points), certificate or title of specialist in Oncology Nursing (1 point), research (s) in the field of oncology in the last five years (3 points), authorship in at least two articles in the last two years on cancer (3 points), experience in AT and oncology of at least three years (3 points).[16]

After the search, a total of 40 eligible judges were reached. They received an invitation letter by email, with a deadline of up to 20 days for the return of the tool; In addition to the Informed Consent Form (ICF), with the appropriate instructions to perform the analysis and assessment. The tool to be filled in for the assessment was built on the Google Docs tool, with initial participant characterization information and tool items. Each item had a space in which judges could provide suggestions for change and improvement.

This process was conducted by the Delphi technique. In this way, the experts answered, through rounds, an evaluative questionnaire. Of the 40 possible judges initially selected, 13 agreed to participate in the bundle assessment, corresponding to the first round (Delphi I), when there were suggestions of alteration in the material for its improvement. The modifications considered pertinent and, after adjustments, the feedback of the answers was sent along with the protocol, configuring the second round (Delphi II), in which nine judges participated (it is noteworthy that these nine judges participated in the two rounds). from Delphi).

For the bundle assessment, the judges' assessments were entered into the Microsoft Excel 2016® database and then analyzed, where the scores attributed to each item were verified. The relevance of the items was obtained by applying the Content Validity Coefficient (CVC).[15] An item with more than 80% agreement among judges (assessed as appropriate) and a Content Validity Coefficient (CVC)> 0.78 was considered valid.[17]

In addition, a descriptive and inferential analysis (binomial test) was performed. Consensus among judges and CVC scores achieved in Delphi rounds. For this, ρ value 0.05 was adopted as a parameter for statistical significance.

The study was approved by the Research Ethics Committee of the *Universidade Federal de São João del-Rei*, under Opinion 2.010.532. It is a subproject of an umbrella research entitled "*construção coletiva de protocolos e manuais*" (collective construction of protocols and manuals). It was developed by the research group called "lifecycle oncology" and registered in the research group directory of the Brazilian National Council for Scientific and Technological Development (CNPq - *Conselho Nacional de Desenvolvimento Científico e Tecnológico*).

Note that external validation of the bundle has not yet been performed. It is the elaboration of a tool that, only after its implementation, should be reassessed and promoted the necessary adaptations, giving greater consistency and representativeness to it. Its implementation requires the training of professionals who will use it, followed by periodic assessments of its use.

Results

In the bundle construction, it was evidenced that, to the initial format, no items previously listed were added. The changes made consist essentially of objectivity (the recommendations allow the desired objective to be achieved), simplicity (the items express a single idea and allow proper understanding), clarity (the content is clearly and unambiguously explained), in accuracy (each item of the tool is distinct from the others, not to be confused) and in the modality (vocabulary is adequate, without generating ambiguities). They resulted in increased

agreement. The completed bundle had 57 items distributed in both modules (Annex 2).

In the assessment process, the expert committee was composed of 13 professionals in the first round of assessment and nine in the second, with loss of two due to non-return of the tool. Doctors with practical experience in oncology and teaching participated, minimum age of specialists was 35 years and maximum 58 years (mean=40.12 and standard deviation=6.75 in Delphi I; mean=42.71 and standard deviation=7.80 in Delphi II), whose mean formation time was 20.20 and standard deviation=5.81 in Delphi I; mean=19.64 and standard deviation=5.84 in Delphi II. They practiced the profession in four of the three Brazilian regions (Table 1).

Table 1. Characterization of the judges participating in the Delphi I and Delphi II phases

Judge characterization	Delphi I (n=13) n(%)	Delphi II (n=9) n(%)
Gender		
Male	2(15.4)	2(22.2)
Female	11(84.6)	7(77.8)
Area currently working		
Teaching	8(61.5)	7(77.8)
Assistance and Teaching	4(30.8)	1(11.1)
Teaching and Management	1(7.7)	1(11.1)
Nursing graduation time		
11 to 20 years	7(53.6)	5(55.6)
21 to 30 years	5(38.7)	3(33.3)
Greater than 30 years	1(7.7)	1(11.1)
Working time in Oncology		
Up to 10 years	1(7.7)	1(11.1)
11 to 20 years	6(45.9)	4(44.5)
21 to 30 years	5(38.7)	3(33.3)
Greater than 30 years	1(7.7)	1(11.1)
Region in which it operates		
Southeast	11(84.6)	8(88.9)
Northeast	1(7.7)	1(11.1)
South	1(7.7)	0(0.0)

Table 2 describes the final consensus among judges on the analyzed items of prevention bundle content before extravasation of AA, which obtained agreement ("adequate" and "totally adequate"), according to Pasquali's assessment criteria.

As shown in Table 2, it was observed that it was below the recommended in preventive measures/actions for the bundle to be considered valid in Delphi I the items: for the patient, only the requirement regarding the modality (69.2%); regarding adequate device for puncture, the items clarity (69.2%) and accuracy (76.9%); Regarding the venous access puncture site, the items simplicity (53.8%), clarity (69.2%), accuracy (76.9%) and modality (69,2%); regarding antineoplastic infusion, the items objectivity (53.8%), simplicity (76.9%) and clarity (76.9%); As for the nursing staff, the modality requirement (76.9%). It is noteworthy that the aforementioned items did not present statistical significance in the agreement among the judges. It should be noted that the suggestions of the judges in the first round (Delphi I) for the items that needed to be reviewed were regarding their presentation, exclusion, relocation or condensation. In the prevention bundle, the requests made were: in the prevention measures "as for the patient", the vocabulary was adequate in order not to generate ambiguities (in letter a it was explained what the possible dermal alterations).

In the "device" actions, the content was clearly, unambiguously and relevantly stated (united in a single item - letter D - giving preference to flexible material catheters such as polyethylene, siliconized, Vialon™ and never using needle catheter for peripheral vesicant administration of AA). In the items "as to the venous access puncture site", there was reallocation and condensation to enable the expression of a single idea, allow proper understanding and adequacy of vocabulary, without generating ambiguities (in letter d, all ten important points were selected for site selection for peripheral venous catheter insertion and reallocated in separate letter); (f) - flushing (catheter pressure washing) with 0.9% saline solution immediately after insertion to test its functionality and during infusion, observe local edema and local pain report by patient). With regard to "infusion" of AT, the recommendations allowed the desired goal to be achieved and modification of the administration of antiemetics was indicated only after AT, and this item was removed due to lack of concise evidence. In the actions "regarding the nursing staff", the vocabulary was correct, so that it did not generate ambiguities. In Delphi II, all requirements presented agreement above 80.0% and were statistically significant ($\rho \leq 0.05$), regarding the agreement among the judges. Again after the judges' suggestions (Delphi II), only the "de-

Table 2. Consensus among the judges in the Delphi I and II stages for the assessed items of the prevention bundle content before antineoplastic agent extravasation in adult cancer patients

Items	Actions/Preventive Measures									
	Regarding patients		Regarding device		Regarding puncture site		Regarding infusion		Regarding the nursing staff	
	Delphi I (ρ value*)	Delphi II (ρ value*)	Delphi I (ρ value*)	Delphi II (ρ value*)	Delphi I (ρ value*)	Delphi II (ρ value*)	Delphi I (ρ value*)	Delphi II (ρ value*)	Delphi I (ρ value*)	Delphi II (ρ value*)
Behavior	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**
Objectivity	92.3% (0.003)**	100,0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	53.8% (0.70)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Simplicity	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	53.8% (0.70)**	100.0% (0.00)**	76.9% (0.16)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Clarity	84.6% (0.02)**	100.0% (0.00)**	69.2% (0.40)**	88.8% (0.009)**	69.2% (0.40)**	100.0% (0.00)**	76.9% (0.16)**	88.8% (0.009)**	84.6% (0.02)**	100.0% (0.00)**
Relevance/ pertinence	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Accuracy	84.6% (0.02)**	100.0% (0.00)**	76.9% (0.16)**	100.0% (0.00)**	76.9% (0.16) **	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Variety	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	88.8% (0.009)**	84.6% (0.02)**	88.8% (0.009)**	84.6% (0.02)**	100.0% (0.00)**
Modality	69.2% (0.40)**	100.0% (0.00)**	84.6% (0.02)**	88.8% (0.009)**	69.2% (0.40)**	88.8% (0.009)**	92.3% (0.003)**	100.0% (0.00)**	76.9% (0.16)**	100.0% (0.00)**
Typicality	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Credibility	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Amplitude	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Balance	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**

*Binomial Test; **ρ ≤ 0.05

Table 3. Consensus among judges in the Delphi I and II stages for the assessed items of bundle content of antineoplastic agent extravasation in adult cancer patients

Items	Overall		Specific Conduct		Under use of antidotes and compresses	
	Delphi I (ρ value*)	Delphi II (ρ value*)	Delphi I (ρ value*)	Delphi II (ρ value*)	Delphi I (ρ value*)	Delphi II (ρ value*)
Behavior	84.6% (0.02)**	88.8% (0.009)**	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**
Objectivity	84.6% (0.02)**	88.8% (0.009)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Simplicity	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Clarity	76.9% (0.16) **	100.0% (0.00)**	76.9% (0.16) **	88.8% (0.009)**	76.9% (0.16) **	88.8% (0.009)**
Relevance/ Pertinence	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	88.8% (0.009)**
Accuracy	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Variety	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Modality	76.9% (0.16) **	100.0% (0.00)**	76.9% (0.16) **	88.8% (0.009)**	76.9% (0.16) **	100.0% (0.00)**
Typicality	84.6% (0.02)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**
Credibility	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**
Amplitude	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**	92.3% (0.003)**	100.0% (0.00)**
Balance	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**	84.6% (0.02)**	100.0% (0.00)**

*Binomial Test; **ρ ≤ 0.05

vice" prevention measures needed to be modified, so as to make them clearer, in the item regarding the selection of the peripheral catheter (PC), it was included: allowing a smaller adequate and constant exchange rate and blood flow. Table 3 presents the final consensus among the experts regarding the assessed requirements of the conduit bundle content in relation to Extravasation of AA that reached agreement equal or superior to "adequate", according to Pasquali criteria.

As explained in Table 3, it was found that, in the general and specific conducts and in the use of antidotes and compresses before extravasation of AA, in Delphi I, the items clarity (76.9%) and modality (76.9%) required adjustments. It is noteworthy that the aforementioned items did not present

statistical significance in the agreement among the judges. The judges' suggestions for general, specific and antidote and dressing use were in terms of presentation and relocation, i.e., it was suggested to divide into different steps: report and record any incident involving extravasation of AA; record by photograph the image of the affected area, and for this purpose there must be written consent from the patient. In Delphi II, none of the items had a CVC below 80.0%, all requirements analyzed were statistically significant ($\rho \leq 0.05$) regarding the agreement among the experts. The judges did not suggest changes in Delphi II regarding the conduct of antineoplastic agent extravasation in adult cancer patients. It is noteworthy that at the end of Delphi II, both bundle modules were expressively valid (prevention of extravasation of AA [CVC=0.93] and conducts before extravasation) [CVC=0.96]).

Discussion

The construction and assessment of the content of a prevention and management bundle before the extravasation of antineoplastic agents in adult cancer patients was developed with methodological rigor. This will enable scientific knowledge to be accessible to nursing professionals working in these spaces.

It is recognized that the absence of a centralized recording of AT extravasation events contributes to the documented low incidence.[4,8] As the amount of extravascular extravasation increases, the cutaneous damage resulting from extravasation of AA is less likely to heal.[18] Thus, delays in extravasation detection can lead to severe skin damage, making detection as early as possible, and the nurse is responsible for the infusion of AT, prevention and management of extravasation.[1,3,19]

Given this conjuncture, the construction and assessment of the bundle developed in this study for the prevention and management of extravasation of AA in adult cancer patients in the most diverse oncological contexts is of paramount importance.

To the initial format were not added items of the initially listed. This infers that the experts considered the prevention and management of extravasation of AA verifications sufficient. The recommendations allowed to achieve the desired objective, besides the increase in the agreement and reliability of the tool.

Of the 57 items distributed in the first module (extravasation of AA prevention measures); the alterations made consisted of clarity (in the items related to the appropriate puncture device, venous access puncture site and antineoplastic infusion); in modality (in the items regarding patients, the nursing staff and the venous access puncture site), accuracy (in the items related to the appropriate device for puncture and venous access puncture site), simplicity and objectivity (both local requirement for venous access puncture). In the second module, concerning the general, specific and the use of antidotes/compresses in relation to extravasation of AA, the changes were related to the clarity and modality of the items.

Regarding the level of scientific evidence of bundle items, most publications were derived from a single descriptive and/or qualitative study (level VI - 54.3%). None evidenced derived from systematic review or meta-analysis of randomized controlled trials (level I) and from well-designed randomized controlled clinical trial (level II). This may suggest that extravasation management is based on descriptive studies; however, the lack of clinical trials can be elucidated by the complexity of ensuring legitimacy and reliability, the diversity of variables and especially the ethical considerations that make the existence of a control group. In addition to the sample size assumptions for quantitative research of this nature, in order to produce statistically significant results due to the relatively low number and sporadic AT extravasation event, making this type of study impracticable.[6,8]

In this study, we highlight the significant experience of the judges participating in the assessment stages, who were doctors with high practical experience in oncology and teaching. In this sense, the literature states that masters and doctors are largely responsible for enabling repercussions on practices and, consequently, on the advancement of nursing.[20]

From this perspective, a study points out that Brazilian nurses with some kind of *stricto sensu*

graduate study fit into a reality that is driven by policies that consolidate and bring innovations in their actions to obtain expressive educational, sociopolitical and scientific-technological impacts for nursing and for health.[21] Thus, it is understood that the participation of experienced professionals involved in research and care is relevant for the assessment of tools to be applied in practice, as this study proposed to assess a bundle in the management of extravasation of AA by nurses.

The assessment process involved the participation of 13 judges in Delphi I (DI) and nine of these judges in Delphi II (DII). Reliability and validity are prime criteria for assessing the quality of a tool. In the meantime, validity is related to the fact that a tool measures precisely what it intends to measure.[18] Reliability is the ability to reproduce a result congruently. This is one of the main quality criteria of a tool.[18,20]

With regard to the Delphi technique used to acquiesce in consultation with a group of expert judges, it has achieved the goal of not deducing a simple answer or reaching consensus alone, but obtained quality opinions and answers for a given question presented to a panel of experts, as recommended by the methodological framework.[12]

In the bundle assessment, the judges presented a significant coefficient of agreement in all assessed items, in order to make the tool valid in relation to behavior, objectivity, simplicity, clarity, relevance, accuracy, variety, modality, typicality, credibility, amplitude and balance.[17]

The suggestions of the judges in the AT extrusion prevention bundle, the requests made in the prevention measures "regarding patients", were the vocabulary adequacy and, in the action related to the risk factors, the dermal alterations were exemplified. that may be present, such as altered edema, dehydration, tone and elasticity.

Proper identification of potential extravasation factors is important to minimize the risk in some patients. In case of increased risk of extravasation, preventive measures should be encouraged or, in some cases, the insertion of a central venous access device should be considered. These factors can be classified into risk factors associated with the patient and the procedure.[2]

In the preventive measures "as to the device" and "as to the venous access puncture site", the judges' suggestions were to unite, reallocate and condense items, to allow the expression of a single idea and proper understanding without generating ambiguity. In the actions "regarding the nursing staff", the vocabulary was adequate. The literature points out that, in the construction of protocols and/or bundles, the adequacy of vocabulary is essential, should be constructed in order to avoid words of little application in the work process.[20,22]

Regarding the actions "regarding infusion" of AT, it was recommended to remove the item: perform administration of antiemetics only after AT, due to the absence of scientific evidence. AT-induced nausea and vomiting may be classified as acute, late or anticipatory, according to the time of onset of symptoms and, for the appropriate choice of antiemetic, the emetogenic level of AA used and the specific risk factors of the drug should be considered. patient, and associations may be used. Several guidelines recommend prophylactic antiemetic regimens for nausea and vomiting.[23]

The judges' suggestions for general, specific, and antidote and compressive conduct were how much to divide the item to report and record any incidence involving extravasation of AA. The action records, through photography, the image of the affected area, and for this purpose there must be written consent of the patient.

It is emphasized that each incident of extravasation must be documented and reported correctly. Photographic documentation is very useful for follow-up and decision-making procedures. The patient should be informed of the scope of the problem if a vesicant AA has extravasated, information about the time involved in the resolution, as well as the legal implications.[2-4,6]

The literature indicates that an acceptable coefficient of agreement among the members of the expert committee should be at least 0.80 and preferably greater than 0.90,[18] as found in this study (prevention of antineoplastic extravasa-

tion [CVC=0.93]. Conducts before extravasation [CVC = 0.96]) and such variations were statistically significant (ρ≤0.05). This proves to obtain better consensus associated with tool improvements between Delphi rounds, and the tool is suitable for reliable application in practice.

Despite the rigor of bundle content assessment, it is necessary to proceed with the following steps, for operational equivalence and measurement. To this end, its application was started in a large Brazilian hospital qualified as a Center for High Complexity in Oncology (CACON), in order to be able to verify its efficiency.

The limitation of this study is related to the low number of expert responses. However, it is noteworthy that the sample of judges was constituted of a number considered adequate by the methodological reference used.[12]

Nevertheless, this study will substantially contribute to reinforce nurses' attention regarding prevention and management of antineoplastic agent extravasation in adult cancer patients.

Conclusion

The results obtained in the study of the construction and assessment of the prevention and management bundle regarding the extravasation of antineoplastic agents in adult cancer patients indicated acceptable psychometric properties for its use in cancer health services. Judges' consensus provided evidence for bundle reliability, with changes to the items they recommended. The assessment of the tool was measured with significant outcome, following the methodological rigor of the Delphi technique.

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Collaborations

Melo JMA, Oliveira PP, Rodrigues AB, Souza RS, Fonseca DF, Gontijo TF, Silveira EAA declare that they contributed to the project design, data interpretation, relevant critical review of the intellectual content and approval of the final version to be published.

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Annex 1. References used as foundation for bundle construction

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Prevention bundle and conducts before the extravasation of antineoplastic agents		
Prevention Before the Extravasation of Antineoplastic Agent (AA)		
CONDUCT	**Actions/Measures**	**Level of Evidence**
REGARDING PATIENTS	Beware of risk factors: presence of tortuous veins, low caliber, obesity, multiple previous venous punctures, presence of dermal alterations (edema, dehydration, altered tone and elasticity), medication use, nutritional alteration, patient movement (limit as much as possible), unconsciousness and sensory demotion.	VI
	Explain to the patient the possible risks related to AA infusion, including vulnerability to extravasation.	V
	Inform about the consequences of extravasation of AA, as well as the prevention methods.	V
	Advise the patient to report any level of pain, burning, tingling or itching, which suggests perceptive infiltration.	V
	Constantly monitor the patient throughout the AA infusion period for signs and symptoms of extravasation beyond pain, as the pain threshold differs from person to person (never underestimate the patient's complaints of local manifestations).	V
REGARDING DEVICE	Request the implantation of central venous access in cases of difficulties in obtaining peripheral venous access (requires up to three attempts to insert the peripheral catheter), as well as prolonged treatment. In the new recommendations of ANVISA the limit for peripheral puncture attempts is three.	VI
	Opt, whenever possible and together with the doctor, the use of central venous catheters (CVC), as they are reliable, produce less discomfort and reduce the risk of extravasation.	VI
	Select a peripheral catheter (PC) that enables lower exchange rate and adequate and constant blood flow. Should be used the one with reduced caliber, and its insertion should be made in the largest caliber vein available. The use of 22G or 24G siliconized needle PC (Abocath®, Jelco®, Saf-T-Intima™) PC is recommended.	VI
	Give preference to catheters of flexible materials such as polyethylene, siliconized, Vialon ™. Never use a needled catheter (scalp®) for peripheral vesicant AA administration.	VI
REGARDING PUNCTURING SITE	Select insertion site of peripheral venous catheter, if applicable, considering safety, reduced risk of extravasation and easy visualization, the most suitable sites for puncture are the forearm veins	VI
	Avoid puncturing: veins of the back of the hand (reduced layer of subcutaneous tissue, proximity to tendons, bones and joints); veins located in the antecubital fossa (proximity to neurovascular structures); veins of the lower limbs	VI
	Insert the peripheral catheter, considering the direction from distal to proximal	VI
	Select the site for peripheral venous catheter insertion considering: (1) venous network characteristics (small and/or superficial veins to be avoided); (2) age of the patient; (3) presence of diabetes; (4) steroid use; (5) anterior peripheral venous catheterizations; (6) bruises; (7) previous and recent hospitalization; (8) dissection of axillary lymph nodes or lymphedema; (9) vascular diseases in the chosen limb; (10) presence of diseases that alter the sensory tactile perception of the limb.	VI
	Perform stabilization and safe catheter coverage using sterile transparent film and aseptic technique, making the puncture site as visible as possible	IV
	Perform flushing (catheter pressure washing) with 0.9% saline solution immediately after insertion to test its functionality. During the infusion observe local edema and local pain report by the patient	IV
	Strictly monitor the infusion site every 5 to 10 minutes	VI
	Avoid the infusion of vesicants for more than 30 to 60 minutes by testing if access is obvious every 5 minutes during administration	VII
REGARDING INFUSION	Infuse AA into a line system without the use of pressure infusers or infusion pumps, as these may increase the risk of extravasation injury due to increased pressure in the inner layers of the veins	VII
	Perform flushing (catheter pressure washing) with 0.9% saline solution after completion of administration	VI
	Consider the administration of drugs that are incompatible and/or may cause synergism or antagonism between them and if necessary to change the equipment	VI
	Obtain blood return prior to AA administration, ensuring correct and safe catheter placement.	VI
	Administer vesicant drugs by means of gravity equipment or by bolus. Never use infusion pump.	VII
	Organize the AA infusion session so that when vesicant antineoplastic is prescribed this is the first to be administered, thus minimizing the risk of extravasation.	VII
	Administer the AA slowly, allowing their progressive dilution in the blood. Never accelerate the infusion.	VI
	Make the selection of appropriate equipment, such as equipment and extenders.	VI
	Infuse 0.9% saline every 5 minutes concomitantly with AA bolus administration, thus avoiding peak concentrations of these drugs in contact with the endovascular wall.	VI
REGARDING THE NURSING STAFF	Promote the permanent qualification of nursing team professionals working in the administration of AA (emphasizing prevention and management of extravasation). Compliance with the manufacturer's recommendations for each medicinal product should be ensured.	IV
	Regularly update the rules and policies regarding the administration of vesicant AA.	VI
	Standardize venipuncture technique and correct indication of vascular access devices.	VI
	Standardize the dilution and infusion rate of the drug.	VI
	Document in the chart all the steps of the AA session. Include records of the patient's condition before, during and after receiving the AA, guidance given, venous catheter insertion site, access conditions, latency (extravasation response period) and patient responses, as well as extravasation, if any.	VI
	Build and implement, jointly with doctors and pharmacists of the service, risk reduction strategies and minimization of damage related to the infusion of vesicants and irritants.	VI
Conducts Before the Extravasation of Antineoplastic Agents (AA)		
General Instructions		
STEPS	**Actions/ Measures**	**Level of Evidence**
1	Remember that after prevention, immediate recognition is the second best measure in treating extravasation of AA.	IV
2	Beware of signs and symptoms of extravasation that include edema, hyperemia, and/or local discomfort, often described as a 'burning' sensation. Other evidence that may indicate extravasation of AA include the presence of resistance to drug introduction into the pathway, slow infusion of the drug into the vascular network, and absence of venous catheter blood return.	VI
3	Identify the extravasation of AA, then immediately stop the infusion.	IV

Continue...

Continuation.

4	Promptly communicate the event to the nurse responsible for the sector.	VII
5	Aspirate 3 to 5 ml of blood with the cannula still at the infusion site.	IV
6	After aspirating the cannula, it should be investigated for specific antidotes and administered as appropriate according to the recommendations in the following table (Specific Instructions). Antidotes should be administered within the first hour after extravasation has been identified. Administration of antidotes should be topical (around the site of extravasation), subcutaneously, intravenously or topically as directed or prescribed by a doctor.	III
7	Keep the compromised limb elevated in order to maintain absorption and drainage of loculated extravasated fluids.	IV
8	Promote cooling or heating of the compromised site according to the specific instruction table for at least 15-30 minutes four times a day for 24-48 hours.	VI
9	Report and record any incident involving extravasation of AA. The record should include the date and time of the incident, the patient's name, the name of the drug, the characteristics of the infused solution, the route of infusion used, the description of the characteristics of the compromised area, the signs and symptoms present and the management. accomplished. It is suggested to record, through photography, the image of the affected area, and for this purpose there must be written consent of the patient.	VI
10	Record by photograph the image of the affected area, and for this purpose there must be written consent of the patient. This action helps in tracking the progress and healing process of the potential injury.	IV
11	Strictly monitor the extravasation site within the first 24 hours after the incident, following follow-up as needed, assessing signs of pain, hyperemia, edema, ulceration or necrosis, depending on the extent of tissue damage	VI
12	When extravasation is suspected, the patient should be monitored by telephone 1 to 3 days after the incident. If the caller suspects complications based on the patient's report, it is recommended that the patient be referred to the referral outpatient clinic for specialist assessment. When extravasation has been confirmed, follow-up appointments should be arranged to assess the site at 2, 5, 7, 14, and continue until the patient is fully recovered.	III
13	Notify the extravasation to ANVISA using the NOTIVISA completed adverse event notification form.	VII
Hot and cold antidotes/compresses application method		**Level of Evidence**
1. **Hyaluronidase** by subcutaneous injection. Administer 150-900 IU around the extravasation area, i.e., administer 1 mL of hyaluronidase solution in five 0.2 mL subcutaneous injections at the extravasation site using a 25 gauge or smaller needle, changing the needle for each injection. .		VI
2. **Sodium thiosulfate**: to prepare a 1/6 molar solution, mix 4 mL of 10% sodium thiosulfate with 6 mL of sterile water for injection. Inject the solution at the extravasation site using a 25 gauge or smaller needle, changing the needle for each injection.		III
3. **Topical DMSO** (99%) apply topically to the skin twice the size of the infiltration with a cotton swab and let it dry (do not cover). Start as early as possible (preferably within the first 10 minutes). Should be applied every 8 hours for 7 days.		III
4. **Dexrazoxane:** this is the only treatment that has been approved by the European Commission and approved by the US Food and Drug Administration for the treatment of anthracycline extravasation. Administer intravenously into a vein in an area away from the extravasation site. Infuse 1,000 mg/m^2 within 6 h of extravasation on Day 1, 1,000 mg/m^2 on Day 2 and 500 mg/m^2 on Day 3. The maximum daily dose is 2,000 mg.		III
5. **Heat treatment**: the application of **cold compresses** is based on the induction of vasoconstriction with consequent decrease of the diffusion rate of the drug within the tissues, reducing the area of potential tissue damage. **The mechanism of heat action applied to the extravasation site** is to induce vasodilation and, consequently, to facilitate increased absorption and systemic distribution of the cytostatic drug.		VI
6. **Hot compress** should be applied for 20 minutes, 4 times a day for 1 or 2 days only for AA classified as **Vinca Alkaloids** and **Oxaliplatin**.		VI
7. Patients should be instructed to pack ice pack or **cold compress** for 15 to 20 minutes, 4 times a day for the first 24 hours for irritants AA.		VI