1312 POSTER

Content Analysis of Pamphlets Provided by Pharmaceutical Companies for the Medical Usage of Oncology Pharmaceuticals

M. Saito[1], Y. Ryushima[1], K. Yonemori[2], A. Hirakawa[3], R. Nishigaki[1], Y. Makino[1], N. Yokote[1], M. Ando[2], Y. Fujiwara[2], H. Yamamoto[1]. *[1]National Cancer Center Hospital, Division of Pharmacy, Tokyo, [2]National Cancer Center Hospital, Division of Breast and Medical Oncology, Tokyo, [3]Tokyo University of Science, Division of Management Science, Tokyo, Japan*

Background and purpose: Patient information pamphlets containing drug information are educational and improve knowledge on dosage, adverse effects, and drug interactions. These pamphlets are provided by pharmaceutical companies and are convenient and appropriate; they are provided free of cost. However, these pamphlets differ in content and the volume and quality of data provided for each drug. In this study, we researched the structure and content of pamphlets produced and distributed by pharmaceutical companies in Japan for chemotherapy drugs.
Material and Method: We collected pamphlets for chemotherapy drugs at 96 components and 116 pharmaceutical drugs; pamphlets for generic drugs were not included in the study. These pamphlets had been produced and distributed between March 1962 and August 2010. We analyzed the pamphlets with regard to dosage form; mechanism of action; and total number of pages, i.e., volume of data.
Results: There were published patient 74 information pamphlet of chemotherapy in 55 of the 116 drugs. The median number of content pages in the pamphlets was 31 (range, 6–101 pages). We obtained a total of 43 pamphlets for 30 of the 71 drugs in the injectable dosage form and 33 pamphlets for 25 of the 42 drugs in the oral dosage form. We obtained 41 pamphlets for 28 of the 77 drugs that had a cytotoxic mechanism of action, 25 pamphlets for 18 of the 21 molecular-targeted drugs and 8 pamphlets for 8 of the 8 hormone preparation. The content of adverse effects was included in all pamphlets. On the other hand, the content of coping strategies for the adverse effects was included 69% (51/74 pamphlets) of pamphlets. Especially, all pamphlets of the hormone preparation had no content of coping strategies for those. The content of coping strategies for those significantly correlated with the dosage form ($p < 0.05$) and mechanism of action ($p < 0.001$).
Conclusion: Our results showed that the patient information pamphlets of chemotherapy were not enough published in Japan. The contents of the patient information pamphlets are expected to be included equally regardless of dosage form or mechanism of action. Therefore it would be required to accumulate and assess clinical information of adverse effects for chemotherapy agents, especially for molecular-targeted drugs, and to reflect in the patient information pamphlets of chemotherapy.

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Stability of Diluted L-asparaginase in Normal Saline Solution

O. Nicolson[1], B. D'Hayer[1], V. Vieillard[1], S. Dolet[1], A. Astier[2], M. Paul[1]. *[1]Henri-Mondor University Hospital, Department of Pharmacy, Créteil, [2]School of medicine Paris 12, Department of Pharmacy -UMRS CNRS 7054, Créteil, France*

Background: L-asparaginase (L-asp; Kidrolase®) is a homotetrameric enzyme used in the treatment of leukemia. However, its practical stability and optimal storage conditions have not been studied in detail. The aim of this study was to assess physical, chemical and biological stabilities of diluted L-asp stored during 10 days at 4ºC.
Materials and Methods: The following methods were used: size exclusion chromatography (SEC), dynamic light scattering (DLS) describing submicronic populations and corresponding mean diameters (md), turbidity (350 nm), thermal aggregation curves and determination of L-asp concentration by UV at 280 nnm (chemical stability) and enzymatic activity (biological stability). Three batches were prepared under aseptic conditions in normal saline (80 μg/ml) in Feeflex® bags and stored at 4ºC during 10 days. Aliquots were taken at days D0, D1, D3, D4, D7, 9 and D10. Results were expressed as mean±SD.
Results: No significant difference was found both for chemical and biological activities after 1 week. The melting temperature was unchanged (59.0ºC). Turbidity exponentially increased from 0.08 to 0.06 absorbance unit, indicating slight aggregation. Immediately after reconstitution, 4 peaks were found by SEC. The mean peak (tetramer 133 kDa, 84% ± 1% of the total area under curve) decreased to 70.4% ± 7.9 after 10 days. These results were confirmed by DLS analysis since 3 initial submicronic populations were found: tetrameric population: md = 9.43±0.3 nm: 99.5% of the total population; highly aggregated populations: 50 < md < 200 nm; 0.5%. After 10 days, the md of main peak was unchanged but the percentage of tetramer decreased to 97.4% with an increase of the md of others populations (up to 900 nm). Percentages of aggregated enzyme (1.4%) remained unchanged during 8 days but reached to 9.5% at D10. However, the loss of enzymatic activity was only 5.1% after day 10, suggesting that aggregated enzyme should partially retain asparaginase activity. In total, our results suggest that the loss of activity was no significant modified until 8 days.
Conclusion: The results show that diluted L-asp in normal saline solution remains stable for 7 days at 4ºC. Therefore, anticipated ready-to-use bags could be prepared by centralized pharmacy units and stored during 1 week without loss of activity. However, the slight increase of aggregates observed during the storage remains questionable in terms of potentially increased immunogenic-induced side-effects.

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Quality of Reporting of Modern Randomized Controlled Trials in Oncology

J. Peron[1], G. Pond[2], H.G. Gan[3], E.X. Chen[4], D. Maillet[1], B. You[1]. *[1]Hospices Civils de Lyon − Centre Léon Bérard, Rhône, Lyon, France; [2]Department of Oncology McMaster University, Ontario, Hamilton, Canada; [3]Austin-Ludwig Cancer Unit Austin Hospital, Victoria, Melbourne, Australia; [4]Department of Medical Oncology and Hematology Princess Margaret Hospital University Health Network, Ontario, Toronto, Canada*

Background: Manuscript quality influences the knowledge translation capability of results from randomized clinical trials (RCTs). The CONSORT statement (Consolidated Standards of Reporting Trials) defines requirements for RCTs publication meant to ensure quality of reporting. The aim of this study was to assess the reporting quality of modern oncology RCTs and to identify characteristics predictive of manuscript quality.
Patients and Methods: A search of MEDLINE was conducted for all oncology phase III randomized clinical trials published in 10 leading medical journals between 2005 and 2009. The quality of every published RCT was assessed using an 18-point overall reporting quality score (OQS) based on the 2001 revised CONSORT statement. Multivariate linear regression was used to identify trial features prognostic for quality of reporting. Furthermore every RCT was assessed using an adjusted 27-item OQS based on the 2010 revised CONSORT statement to provide baseline data for future evaluations of manuscript quality.
Results: 357 RCTs with a median of 437 patients each were reviewed. The number of published RCTs decreased from 91 in 2005 to 53 in 2009. They were published in intermediate (<10: 27%), high (10−20: 59%) or very high (>20: 14%) impact factor (IF) journals. Pharmaceutical companies funded, at least partially, 61% of trials. Median 2001 OQS was 14 on a 0−18 scale while median 2010 OQS was 19 on a 0−27 scale. Just over 1/3rd (120) reported 12 or less items on the 2001 OQS. Poorly reported items included: method used to generate the random allocation (n = 104; 29%), whether and how blinding was used (n = 146; 41%), method of allocation concealment (n = 182; 51%) and participant flow (n = 212; 59%). A high IF ($p < 0.001$) and a recent publication date ($p = 0.004$) were the 2 independent favorable prognostic factors identified in a multivariate model. There was no impact of source of funding, geographical origin of RCTs, tumour site, treatment setting and positivity of trial results. Trials sample size was borderline significant if included in the multivariate analysis ($p = 0.115$).
Conclusion: The overall quality of RCT reporting improved from 2005 to 2009 according to 2001 CONSORT criteria, however, a number of items remained unreported in many trials. High IF journals were more likely to report RCTs adequately.

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Content Analysis of "the Guidance for Proper Usage" That Are Distributed to Medical Oncologists for Promoting Oncology Pharmaceutical Safety

K. Yonemori[1], A. Hirakawa[2], Y. Ryushima[3], M. Saito[3], H. Yamamoto[1], T. Hirata[1], M. Ando[1], H. Yamamoto[3], Y. Fujiwara[1]. *[1]National Cancer Center, Medical Oncology Division, Tokyo, [2]Tokyo University of Science, Management Science, Tokyo, [3]National Cancer Center, Pharmacy Division, Tokyo, Japan*

Background and purpose: Oncology pharmaceuticals such as cytotoxic agents, molecular-targeted agents, and hormonal agents are used for treating solid and hematologic malignancies. Pharmaceutical companies often provide a unique guidance for proper usage to medical oncologists to facilitate proper usage of the approved drug. In this study, the revelation of the guidance for proper usage in clinical practice has been assessed.
Material and Method: Among approved oncology drug in Japan, we collected guidance for proper usage for oncology pharmaceuticals; these guidance had been published by pharmaceutical companies for medical oncologists in Japan. For each guidance for proper usage, we determined the total number of pages and the proportion of pages that discussed toxicity, drug information, and the results of clinical trials.