SHORE-C
Sussex Health Outcomes Research & Education in Cancer

Diarrhoea Management Diary

Introduction: There are many causes of loose, watery stools that characterise diarrhoea including infection, neuroendocrine tumours in the gut, stress, anything that alters normal gut flora including surgery, radiotherapy and certain medications such as antibiotics. Many drugs used in cancer especially those containing fluoropyrimdines and the tyrosine kinase inhibitors cause troublesome diarrhoea that can be serious enough to merit hospitalisation, lead to dose readjustments or discontinuation of treatment. Chronic diarrhoea can also cause pain, significant skin soreness, a diminution of activities of daily living all of which has a deleterious effect on a patient's overall quality of life.

Medical management of treatment related diarrhoea (TRD) can be multi-faceted and ranges from simple advice regarding diet (eg dietary restrictions or the bananas, rice, apples and white toast diet, BRAT diet) to over-the-counter and prescribed medications including loperamide, diphenoxylate-atropine sulphate, or maybe even opioids such as codeine. These approaches are of variable efficacy and long-term use may create other problems.

Patients with uncontrolled diarrhoea may try other strategies, which they may or may not reveal to their healthcare providers. The simplest and most effective of these is to just stop taking their drugs and non-adherence or sub-optimal adherence to oral medication is common.
There are useful tools available to measure the overall effect that diarrhoea may have on a patient's physical, functional, emotional and social well-being such as the FACT-G (Webster et al. 2003) with its diarrhoea subscale (FACIT-D).

The primary aim of the DMD is somewhat different and is designed to capture some of the ways in which patients might attempt to manage or control the TRD that they experience when taking medicines prescribed for conditions such as cancer. The DMD could be used to assist with the clinical evaluation of supportive TRD strategies as part of the clinical record for individual patients or it could be employed within research trials testing new management approaches.

Development: Preliminary development of the DMD and testing of the items was carried out according to the principles of good practice for the translation and cultural adaption process for PROs described by the ISPOR Task Force (Wild et al. 2006). A literature search was performed using Medline and Scopus to assess information about TRD symptoms, self-management strategies for diarrhoea, and existing questionnaires for TRD, disease-related diarrhoea or bowel dysfunction. The retrieved publications covered a broad range of instruments for various medical conditions, including gastrointestinal diseases, bowel or rectal cancer, and HIV-related diarrhoea.

Selection and origin of items

The selected items for the diary were based on information of retrieved publications and instruments (Atherton et al. 2013, Clark & Talcott 2001, Davidson-Homewood et al. 2003, Haddock

et al. 2007, Temple et al. 2005). The initial DMD contained 10 items with both open and closed format questions relating to stool frequency, consistency and volume (item 1-4), symptom management including dietary changes (item 5-7), anti-cancer treatment (item 8, 9), and an open response option (item 10). Some items contained a 'please specify' option to ensure that as much relevant information as possible was being captured. An open question was added at the end inviting participants to provide extra information in free text format and complement responses to the closed questions (McColl et al. 2001, O'Cathain & Thomas 2004). Two versions of the diary were developed (DMD-version 1A and DMD-1B) each containing the 10 items with different fonts (Arial and Garamond respectively) and lay-outs.

Pilot testing of initial DMD

The original testing of the acceptability of the initial DMD (including both open and closed format questions) was performed in a sample of patients with bowel conditions (e.g. coeliac disease, IBS, IBD, dysentery) or cancer-treatment related gastrointestinal symptoms (n = 7), and in healthy controls (n = 5). The sample was predominantly female (75%) with an average age of 53.6 years (range 37-65). Participants were asked to complete both versions of the questionnaire in counterbalanced order. A standard set of questions was developed for the cognitive debriefing relating to the overall structure and acceptability of the diary, wording of the items and response/scale options, and preference for lay-out and format. Face-to-face or telephone interviews were conducted with all participants, lasting between 20 and 30 minutes.

The results revealed that the initial DMD performed well in cognitive testing. The majority of participants preferred version A because of the clarity and font-size (91%) or lay-out (78%). The DMD demonstrated good face and content validity. The item-analysis showed that all respondents understood the items and that the diary adequately covered issues related to TRD management. No additional items were suggested. All participants indicated that the item order/sequence was well structured. Only minor modifications to the initial DMD were made. One item (relating to stool volume) was removed as patients reported an inability to reliably judge the volume, and the response scales of two items were extended. Other revisions mainly consisted of minor lay-out changes (e.g. line spacing, size/format tick box).

A small-scale field pre-test was conducted in another group of 6 healthy volunteers and the questionnaire was shown again to 2 participants from the original patient group. The 9-item DMD-version 2 was acceptable to all respondents and item response rates were good. No further changes were implemented.

Development of the closed format DMD

A pragmatic decision was taken to produce a closed format version of the DMD (DMD-version 3) for use within international clinical trials due to the difficulty translating free-text responses easily and reliably. Modifications to the DMD (i.e. the open format items only) were based on previous publications about management of treatment-related or chronic diarrhoea (Abdullah & Firmansyah 2013, Benson et al. 2004, Cherny 2008, Morturano 2010, Stein 2010), and the diarrhoea treatment guidelines of the American Cancer Society/National Cancer Institute, Cancer Research UK, the World Health Organisation, and the World Gastroenterology Organisation. Fixed

response options were added to the items relating to changes in diet, use of additional medicines, and advice for diarrhoea management from health care professionals (HCP). Following this the order of items was also changed to improve the flow of the revised version. Internal review within SHORE-C of version 3 resulted in further minor changes (e.g. lay-out, colour) of the diary.

Pilot testing of the closed format DMD

Pilot testing of the DMD-version 4 was conducted in the previous sample of patients with bowel conditions or cancer-treatment related gastrointestinal symptoms (n = 4) and healthy controls (n = 5). Participants were asked to complete the diary again and to provide comments. General feedback was good and no major problems were encountered other than correcting the omission of a sub-question and small additional changes in lay-out to improve clarity which resulted in the DMD-version 5. This version was reviewed internally within SHORE-C and further minor mainly cosmetic adaptations were made. DMD-version 6 was discussed again with 2 participants from the patient group. No further changes were suggested (one participant commented "this questionnaire is virtually perfect").

Following a review by clinical, statistical and data management personnel from GlaxoSmithKlein (GSK) regarding the possible recording of severe adverse events, 2 extra response options to the item covering diarrhoea management advice from HCPs were included. A small-scale field pre-test of DMD-version 7 was conducted in a group of 7 healthy volunteers. All participants completed the diary without problems and no additional feedback was provided.
A final review by GSK resulted in a minor adjustment in the response options of question 1 (DMD-version 8) and rephrasing of question 6 (DMD-version 9) for analysis/translation purposes.

Instructions to patients:

Patients should be asked to complete the DMD-version 9 weekly as items refer to experiences and behaviours over the past week. Patients should be encouraged to be as honest as possible in their responses. They should be encouraged to answer every question and be assured that, if being used within a clinical trial setting, responses will remain confidential to the study team and not seen by their treating physician or stored in hospital notes. Consequently they should be reminded to discuss any issues that completing the DMD has made them think more about with the doctors/nurses treating them. For example the DMD might prompt them to tell medical staff about other medications they have been using.

Scoring/Interpretation: There is no numerical 'score' as such but changes over time for categorical and dichotomous responses can be charted either for 1) an individual showing the trajectory of diarrhoea onset and/or resolution or 2) for groups of patients if used within a clinical trial setting. Simple proportions of patients within groups responding yes or no to relevant questions can be compared.

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