Malignant ascites: systematic review and guideline for treatment

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CRD summary
This review assessed the efficacy of abdominal paracentesis, diuretics and shunting in the management of symptomatic malignant ascites, in order to develop guidelines for treatment. The authors concluded that the evidence to support these common procedures was weak and mainly based on poor study designs. It is important that the authors’ guidelines are interpreted in light of the poor evidence.

Authors’ objectives
To collect, critically appraise and summarise the evidence on the effectiveness of abdominal paracentesis, diuretics and peritoneovenous shunting in the management of malignant ascites, and to develop a guideline in order to get evidence into practice.

Searching
The following electronic databases were searched from inception to August 2005: MEDLINE, Biological Abstracts, BIOSIS Previews, CINAHL, ACP Journal Club, DARE, the Cochrane Database of Systematic Reviews, the Cochrane CENTRAL Register, PubMed and (up to 2002 only) Cancerlit. Details of the search strategy were provided. In addition, reference lists of pertinent articles and chapters on ascites in books on palliative care were handsearched for additional studies.

Study selection
Study designs of evaluations included in the review
Any study design was eligible for inclusion, i.e. non-analytic studies such as case-series were included if this was the best evidence that could be obtained. There were no randomised controlled trials amongst the included studies, and most of the studies were case series.

Specific interventions included in the review
Any abdominal paracenteses, diuretics and peritoneovenous shunts were included. Comparators were not specified nor necessarily required. The included studies reported various numbers of paracenteses (range: 35 to 127). Types of diuretics also varied and included different combinations of intravenous furosemide, intravenous bumetanide, spironolactone and methylcloothiazide. Both Denver and Le Veen peritoneovenous shunts were assessed in the included studies.

Participants included in the review
Adult cancer patients with malignant ascites due to cancer of any type were eligible for inclusion. The included participants had various, usually unspecified, tumours.

Outcomes assessed in the review
The primary outcome measure was the prevention or reduction of fluid accumulation. The secondary outcomes included incidence of adverse events and predictors of response. The authors also reported the percentage symptom relief (variously defined) and the duration of the effect.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The level of evidence was graded according to guidelines of the Scottish Intercollegiate Guidelines Network (SIGN), and this was dependent on the study design and methodology. No further details were provided. Two independent
reviewers assessed the rigour of the study design. It was not stated how any disagreements were resolved.

Data extraction
The authors did not state how many reviewers performed the data extraction. Data on study design, study population (including primary diagnosis and co-morbidities), intervention (i.e. diuretic regimen, number of paracenteses or shunt type used) and outcomes were recorded.

Methods of synthesis
How were the studies combined?
Differences in study design and methodology meant that the studies could only be combined in a narrative.

How were differences between studies investigated?
Differences between the studies were discussed in the text and highlighted in the data tables.

Results of the review
A total of 32 studies (n=849) were included: 1 non-randomised open controlled trial, 5 cohort studies or prospective uncontrolled trials and 26 non-analytic studies (e.g. case series). Three case series (n=43) and 2 prospective uncontrolled trials (n=59) focused on abdominal paracentesis. One non-randomised open controlled trial (n=68), 3 cohort studies (n=43) and 1 case report (n=2) assessed management by diuretics. The non-randomised open controlled trial (n=42) and 21 case series (n=592) assessed management by peritoneovenous shunts.

Symptomatic management by paracentesis.
Three studies show good, although temporary, relief of symptoms related to the build-up of fluid for about 90% of patients managed by paracentesis. There was no consensus on fluid withdrawal speed. Possible complications of paracentesis included secondary peritonitis, pulmonary emboli and hypotension. Repeated large-volume paracentesis without plasma volume expansion may be associated with a significantly higher incidence of hypotension and renal impairment. A significant improvement of symptoms of abdominal pressure occurred with the removal of a few litres (mean 5.3 L, range: 0.8 to 15) without severe side-effects (data based on 1 study).

Symptomatic management by diuretics.
Diuretic use in managing malignant ascites was inconsistent amongst physicians, and the available evidence assessing its efficacy was weak. However, overall, in patients with different tumours, diuretics seemed to be successful in approximately 43% of cases (data based on 5 studies). One study suggested that serum-ascites albumin gradients may provide a useful guide to predict a patient's response to diuretics.

Symptomatic management by peritoneovenous shunts.
Shunt insertion was associated with potential fatal side-effects and considerable costs in terms of time and money. For these reasons, shunts should only be used when other treatment options like diuretics have failed and when the life expectancy of the patient is long enough to derive benefit.

Authors’ conclusions
The authors stated that although paracentesis, diuretics and shunting are commonly used procedures, the evidence is weak. The available data show a good although temporary effect of paracentesis on symptom relief. Fluid withdrawal speed and concurrent intravenous hydration have not been sufficiently studied. Peritoneovenous shunts can control ascites in patients with malignant ascites, but have to be balanced by the potential risks of this procedure. The available data on the use of diuretics to treat malignant ascites are controversial. The use of diuretics should, therefore, be considered in all patients, but must be evaluated on an individual basis.
CRD commentary
This was a very broad review of the topic area. The inclusion of all study designs was necessitated by the poor quality of the evidence base. The authors' conclusions were limited by the fact that only lower levels of evidence were identified. Despite the comprehensive inclusion criteria and the extensive searches of electronic databases, there are some concerns about the robustness of the review methods. The authors failed to report whether any measures were taken to reduce errors and bias in how the studies were selected and data extracted, which may lead to selection bias or inaccuracies in the reporting of data. There also appears to have been little attempt to identify unpublished studies, which may leave the review open to publication bias. Given the potential bias against the publication of poorer study designs and the fact that many of the authors' findings were based on such studies, the potential for publication bias in this review is of concern. However, the authors have rightly stressed in their conclusions that the evidence base is very weak; this is further highlighted by the low evidence gradings supporting their guidelines. It is therefore important that the reader take the authors' evidence gradings and the potential weaknesses of the review methodology into account when interpreting the review findings.

Implications of the review for practice and research
Practice: The authors provided the following guidelines.

Paracentesis is indicated for those patients who have symptoms of increasing intra-abdominal pressure (Grade D recommendation).

When removing up to 5 L of fluid, intravenous fluids do not seem to be routinely required (Grade D recommendation).

Intravenous hydration should be considered if a patient is hypotensive or dehydrated or known to have severe renal impairment and paracentesis is still indicated (Grade D recommendation).

To avoid repeated paracentesis, peritoneovenous shunting may be considered (Grade D recommendation).

Diuretics should be considered in all patients, but this has to be evaluated on an individual patient basis (Grade D recommendation).

The choice and dose regimens of diuretics have not been evaluated (Grade D recommendation).

Research: The authors stated that further studies are required to evaluate the best type and regimen of diuretics. In particular, randomised controlled studies, possibly using a crossover design, are required to compare the use of diuretics with paracentesis. However, crossover studies should only be used in patients who are in a comparatively stable condition in order to avoid introducing variability into the patients' responses over time.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.