



CHBG NEWSLETTER

Cochrane Hepato-Biliary Group (CHBG)

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CHBG REVIEWS AND PROTOCOLS ON THE CLIB ISSUE 1 AND 2, 2002

NEW REVIEWS

1. Emergency sclerotherapy versus medical interventions for bleeding oesophageal varices in cirrhotic patients
2. Interferon for acute hepatitis C
3. Ribavirin with or without alpha interferon for chronic hepatitis C
4. Ursodeoxycholic acid for primary biliary cirrhosis
5. Antibiotic prophylaxis for cirrhotic patients with gastrointestinal bleeding
6. Interferon for interferon naive patients with chronic hepatitis C
7. Propylthiouracil for alcoholic liver disease
8. Sequential combination of glucocorticosteroids and alfa interferon versus alfa interferon alone for HBeAg-positive chronic hepatitis B

UPDATED REVIEWS

1. Somatostatin analogues for acute bleeding oesophageal varices

COMMENTED REVIEWS

1. Terlipressin for acute esophageal variceal hemorrhage

The CHBG received comments and criticism on this Review in November 30, 2001. The reviewers' reply is published in the comments section of the Review in Issue 2, 2002 of The CLib.

NEW PROTOCOLS

1. Artificial and bioartificial support systems for liver failure
2. Beta-interferon for chronic hepatitis B
3. Bile acids for primary sclerosing cholangitis
4. Foscarnet for chronic hepatitis B
5. Gamma-interferon for chronic hepatitis B
6. Interferon for interferon relapsing and non-responding patients with chronic hepatitis C
7. Lamivudine for chronic hepatitis B
8. Levamisole for chronic hepatitis B
9. Milk thistle for alcoholic and/or hepatitis B or C liver diseases
10. Percutaneous needle aspiration with or without oral albendazole for uncomplicated hepatic hydatid cysts
11. Surgical versus medical treatment of refractory ascites
12. Thymosin alpha 1 for chronic hepatitis B
13. Transcatheter arterial chemoembolization for hepatocellular carcinoma
14. Weight reduction for non-alcoholic fatty liver

WITHDRAWN PROTOCOLS

1. Nucleoside analogues with or without alpha-interferon for HBeAg-positive chronic hepatitis

We have withdrawn this protocol from further publication on The CLib with a start from Issue 2, 2002 since a new protocol entitled 'Lamivudine for chronic hepatitis B', prepared by Humberto Saconato et al., is published in Issue 2, 2002. This new protocol partly replaces the nucleoside analogues protocol.

NEW REGISTERED TITLES

1. Antibiotics for cholangitis - Renata Kukuruzovic, Australia
2. Hepatitis B vaccination for chronic renal failure - James Zacharias, Canada
3. Support programs for patients with hepatitis C - Peninnah Oberdorfer, Australia
4. Glucocorticosteroids for primary sclerosing cholangitis - Wendong Chen, Denmark
5. Medicinal herbs for cholelithiasis - Tao Gan, China

6. Glucocorticosteroids for liver transplanted patients - Jan Lerut, Belgium
7. Beta-blockers for primary prevention of oesophageal variceal bleeding in cirrhotic patients - Wendong Chen, Denmark
8. Beta-blockers for prevention of oesophageal variceal rebleeding in cirrhotic patients - Wendong Chen, Denmark
9. Bile acids for prevention of rejection in liver transplanted patients - Wendong Chen, Denmark
10. Bile acids for gallbladder stones - Wendong Chen, Denmark

REVIEWS IN EDITORIAL PROCESS – HOPEFULLY TO BE PUBLISHED IN ISSUE 3, 2002 OF THE CLIB

1. Shunts versus endoscopic therapy for long-term management of variceal haemorrhage
2. Surgical versus endoscopic treatment of bile duct stones
3. Total portosystemic shunt versus shunts preserving portal venous hepatic perfusion for variceal haemorrhage
4. Branched-chain amino acids for hepatic encephalopathy
5. Artificial and bioartificial support systems for liver failure
6. Radiofrequency thermal ablation versus other interventions for hepatocellular carcinoma
7. Ursodeoxycholic acid and/or antibiotics for prevention of biliary stent occlusion
8. Medicinal herbs versus medicinal herbs for chronic hepatitis B virus infection
9. Bile acids for viral hepatitis
10. Anabolic-androgenic steroids for liver disease

PROTOCOLS IN EDITORIAL PROCESS – HOPEFULLY TO BE PUBLISHED IN ISSUE 3, 2002 OF THE CLIB

1. Interferon for hepatocellular carcinoma
2. Endoscopic interventions for unresectable cholangiocarcinoma
3. Percutaneous ethanol injection or percutaneous acetic acid injection for hepatocellular carcinoma
4. Glucocorticosteroids for primary biliary cirrhosis
5. Emergency sclerotherapy or band ligation combined with vasoactive drugs for bleeding esophageal varices in cirrhosis
6. Antibiotics for cholangitis
7. Hepatitis B vaccination for patients with chronic renal failure
8. Glucocorticosteroids for primary sclerosing cholangitis

COMMENTS AND CRITICISMS ON COCHRANE REVIEWS

What happens when comments and/or criticisms are received?

If a reader of *The Cochrane Library* submits a comment or criticism on a review electronically, it is automatically sent to Update Software. The comment will be posted on the public website at (<http://www.update-software.com/comcrit.htm>) unless it is defamatory or trivial. The relevant Group's Criticism Editor and its editorial base will be notified automatically that the comment has been posted on the website. The commentator gets an automatic acknowledgement of their comment, and should receive acknowledgement from the Criticism Editor within one week.

The Criticism Editor will then contact the commentator for clarification if required and pass on the comment to the reviewer of the review for a reply. It is very helpful if the reviewer of the review can acknowledge receipt of the comment. The comment and the reviewer's reply will appear together in the Comments section of the review (as in the Letters section of a paper journal), when they have been pasted in to the review using the headings provided in the Comments field in RevMan 4.1 and then submitted by the editorial base for publication. It is recommended one to six months for the reviewer to reply, with at least an initial response to the comment and how they intend to respond to it (for example, when the review is next updated). Immediate responses to a criticism from the reviewer can also be posted on the website, but are best sent to the Criticism Editor of the Collaborative Review Group to arrange uploading.

If reviewers receive any written comment on their review by other means (such as by letter, fax or published correspondence on the review in a paper journal), please send a copy to the Review Group Co-ordinator so that they can be submitted to the website via the feedback system. If there are many comments on a review it will be up to the Criticism Editor to decide which ones are sufficiently important to incorporate into the Comments section of the review, and which should remain on the website (akin to electronic letters to the *British Medical Journal*).

At present the only place that comments can be archived is on the website, as out of date comments are stripped out of the review on *The Cochrane Library* when an update has made them redundant. It is hoped that a system can be developed to mark comments as active or archived in the future.

This message is sent by Chris Cates, Convener of the Comments and Criticisms Management Group, and is published with abbreviations.

PAST EVENTS

9TH COCHRANE COLLOQUIUM, LYON – FRANCE

Christian Gluud and Bodil Als-Nielsen participated in the 9th International Cochrane Collaboration Colloquium in Lyon, France 9-13 October 2000. They presented four posters.

AASLD MEETING, DALLAS – USA

In November 2001, though the September tragedies in the USA, a CHBG meeting was held during the AASLD meeting. Christian Gluud and Bodil Als-Nielsen were among the speakers. Ronald Koretz and Christian Gluud chaired the meeting. We like to thank all the people who attended it.

BRISTOL MEETING – UK

Christian Gluud and Lise Lotte Kjaergard participated in the formation of the Meta-Epidemiologic Research Group on Bias (MEB) and participated in the founding meeting of the MEB Group in Bristol, UK, November 2001.

VISITS

Andrea Rambaldi, Italy stayed for a week in January at the Editorial Team office and worked on two systematic reviews, i.e., 'Milk thistle for alcoholic and/or hepatitis B or C liver diseases' and 'Anabolic-androgenic steroids for alcoholic liver disease'.

Jesper Brok, Denmark worked for a month in January on the systematic review 'Glucocorticosteroids for viral hepatitis C', which original protocol was published by Martin Mellerup, et al.

Wendong Chen has prolonged his stay at The CHBG Editorial Team office and is working now on five additional protocols for Reviews.

FUTURE EVENTS

CHINA

At 2002 Shanghai International Symposium of Cirrhosis and its Complications from March 27 to March 29, 2002 Christian Gluud is invited to deliver state-of-the-art lecture on 'Evidence-based medicine in hepato-biliary diseases'. Christian Gluud is also invited to do a talk on 'History of evidence-based medicine' at the Chinese Clinical Epidemiology Association. His third lecture will be at The Second Asian-Pacific

Conference on Evidence-Based Medicine that will be run from 7 to 10 April 2002. The conference is organised by the Ministry of Health of China and sponsored by the School of Medicine at West China Hospital, Sichuan University, Chengdu, China. There he is invited to speak on 'The Cochrane Hepato-Biliary Group: achievements and challenges'.

TRAIN THE TRAINERS, CRETE – GREECE

Following the last year's success Christian Gluud is invited again to Crete in April 2002 by Organisation Mondiale de Gastro-Entérologie (OMGE)/Organisation Mondiale d'Endoscopie Digestive (OMED) to teach at the Train-the-Trainers workshop. Two representatives of the national gastroenterologic associations from 20 countries will receive education on evidence-based medicine, The Cochrane Collaboration, and systematic Reviews. A training material has been developed. The reference is:

1. Gluud C. Evidence based medicine, The Cochrane Collaboration and systematic reviews. Organisation Mondiale de Gastro-Entérologie (OMGE)/Organisation Mondiale d'Endoscopie Digestive (OMED) Train the Trainers, Crete 2002 [Review on CD-ROM]. 2002;1-50.

THE EASL 2002 MEETING – SPAIN

The 37th annual meeting of the European Association for the study of the Liver (EASL) will be held from 18 to 21 April 2002 in Madrid. Since 1994, when the second exploratory meeting took place, the CHBG has had regular biannual meetings during the EASL meeting. A full meeting was planned for Madrid with Luigi Pagliaro and Rosanna Simonetti as chairs. However, this year we could not get suitable time to run the 13th CHBG meeting, and we thought that it would be unjustifiable if only few people were present.

The CHBG, however, will be presented with a stand at The EASL 2002 exhibition where again people would learn about the work of the group and its achievements. The aim is also to recruit people for preparation of Cochrane Hepato-Biliary systematic Reviews, find handsearchers of hepato-biliary journals, consumers, and to make more people aware of The Cochrane Library as an evidence-based source. The CHBG acknowledges the sponsorship provided by the EASL secretariat for the stand.

EU-MEETING ON MEDICAL RESEARCH, GRANADA – SPAIN

An EU-meeting on medical research 'Research in the health systems of The European Union: needs and priorities' will be run in Granada, Spain from 8 to 10 May 2002. Christian Gluud is invited to speak on 'Evidence based medicine, its applicability in clinical practice'.

THE EASL 2003 MEETING – TURKEY

The CHBG will hold a meeting in the morning of 28 April 2003 during the 38th annual EASL 2003 meeting in Istanbul.

10TH COCHRANE COLLOQUIUM, STAVANGER - NORWAY

The 10th Cochrane Colloquium will be held from 31 July to 3 August 2002 in Stavanger, Norway. There will be workshops and meetings aimed at meeting the needs of reviewers, editors, review group coordinators, trials search coordinators, consumers, and methodologists. For more information visit <http://www.cochrane.no/colloquium/>.

PUBLISHED ELSEWHERE

AGA TECHNICAL REVIEW ON PARENTERAL NUTRITION

Christian Gluud

Ronald L Koretz, the USA CHBG Editor, in collaboration with Timothy O Lipman and Samuel Klein published a masterpiece of a technical review prepared for the American Gastroenterological Association Clinical Practice and Practice Economics Committee in *Gastroenterology* 2001;121:970-1001. Based on more than 1000 references, this review assesses the beneficial and harmful effects of parenteral nutrition for a number of specific clinical conditions (perioperative; oncology; liver disease; acute pancreatitis; inflammatory bowel diseases; low-birth-weight infants; diarrhoea in infants and children; acquired immune deficiency syndrome; chronic pulmonary disease; chronic renal failure; acute renal failure; burn injury; short bowel syndrome; and other critical illness).

Based on 82 randomised clinical trials included in a 'global' (i.e., including all conditions) meta-analysis, parenteral nutrition (intravenous fluids containing nitrogen plus at least 10 kJ per kg per day of non-protein calories) versus control intervention (ad libitum feeding and/or 5% dextrose intravenously) significantly increased infectious complication rate and did not significantly affect mortality, total complication rate, or duration of hospitalisation. Based on 27 randomised clinical trials included in a 'global' (i.e., including all conditions) meta-analysis, protein-sparing parenteral nutrition (that is nitrogen plus calories infused in amounts that was inadequate to meet daily requirements) versus control did not significantly affect mortality, total complication rate, infectious complication rate, or duration of hospitalisation.

The review then addresses the effects of the two types of experimental interventions for the specific conditions. They draw their conclusions based on patients that are not severely malnourished since data on severely malnourished patients are lacking. In patients with liver diseases (mostly alcoholic hepatitis) only a limited number of trials were found, but there were no significant beneficial effects on any of the outcomes. The authors recommend that parenteral nutrition should be used for low-birth-weight infants without intact enteral function and patients with inadequate bowel function and more than three months life expectancy. Until further evidence is provided, the decision when to treat a severely malnourished patient, is left open to the clinician. The reader is referred to the article for the further recommendations provided by the authors.

The American Gastroenterological Association in the same volume of *Gastroenterology* (2001;121:966-969) endorsed the recommendations of Koretz et al.

If this review is followed, it will not only reduce the number of complications that patients seem to get from parenteral nutrition, but also reduce substantially the expenses used on parenteral nutrition. We need more research on severely malnourished patients – and we look forward to a systematic review on enteral nutrition.

POINTS OF VIEW

ASSESSING METHODOLOGIC QUALITY OF RANDOMISED CLINICAL TRIALS IN SYSTEMATIC REVIEWS: THE JADAD QUALITY SCALE VERSUS SEPARATE COMPONENTS.

Lise Lotte Kjaergard

It is important to consider the methodologic quality of the included trials when performing systematic reviews. Previous evidence¹⁻³ indicates that trials with inadequate or unclear generation of the allocation sequence and inadequate or unclear allocation concealment tend to exaggerate intervention benefits compared with trials reporting adequate randomisation methods. Likewise, randomised trials without double blinding tend to exaggerate intervention effects compared with double blind trials.¹⁻³ These aspects of methodologic quality could be assessed as separate components or combined in composite scales. One of the most popular composite scales was developed by Jadad and colleagues.⁴ This scale includes the generation of the allocation sequence, double-blinding, and follow-up. On average, trials achieving a low score on this scale exaggerate intervention benefits compared with trials achieving a high score.^{2,3} It may be argued that composite scales

including greater sensitivity have several advantages over separate components. However, the Jadad scale has several shortcomings. First, allocation concealment was not included because of the low frequency of endorsement.⁴ However, allocation concealment is an important marker of methodologic quality, which should be considered when assessing methodologic quality. Second, the scale consists of only three components. Double blinding carries large weight in the scale, and overlap between this component and the scale is considerable. Furthermore, some interventions are difficult or impossible to blind. Third, the scale includes the reported follow-up, which has not been associated with intervention effects and primarily concerns the quality of the reporting. Finally, even if authors find a significant association between the quality scale and intervention benefits, analysis of the separate components will still be necessary. Accordingly, assessment of methodologic quality should focus on the separate components generation of allocation sequence, allocation concealment, and double blinding.

1. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;273:408-12.
2. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 1998;352:609-13.
3. Kjaergard LL, Villumsen J, Gluud C. Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Ann Intern Med* 2001;135:982-9.
4. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomised clinical trials: is blinding necessary? *Control Clin Trials* 1996;17:1-12.

USEFUL TO KNOW

- **Search terms or search strategies**

Search terms or search strategies in protocols and Reviews should be sufficiently listed to allow others to run them. We suggest to reviewers to include the search strategies within Published Notes or within an Additional Table in RevMan and refer to them within the text under 'Search strategies for identification of studies'. When writing about the search strategy in the Reviews reviewers should remember that there is almost a standard way of reporting. Data ranges should be given for all databases searched. This applies also for the abstract of the Review. Please check the Reviewers' Handbook Appendix 2a. Guide to the format of a Cochrane Review.

- **Publication agreement**

The following passage is suggested for inclusion in letters of submission to journal editors:
'This systematic Review has been prepared under the aegis of the Cochrane Collaboration, an international organisation that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions. The Collaboration's publication policy permits journals to publish Reviews, with priority if required, but permits the Cochrane Collaboration also to publish and disseminate such Reviews. Cochrane Reviews cannot be subject to the exclusive copyright requested by some journals.'

Please do not forget to enter information if any under 'Other published versions of this review' under References in RevMan.

- **Permission for publication of a figure from a Cochrane Review is also required.**

Reviewers should contact the publishers, Update Software and ask for a standard permission form to complete. If reviewers e-mail <info@update.co.uk> or call telephone +44 (0)1865 513902 they will be sent one.

**THE AMERICAN JOURNAL OF
GASTROENTEROLOGY – CO-PUBLICATION
AGREEMENT**

A publication policy between The American Journal of Gastroenterology and the CHBG was signed in December last year. Reviewers are welcome to send a sister publication of their reviews also to this Journal.

COCHRANE TRAINING WORKSHOPS

At the web address
<http://www.cochrane.org/cochrane/workshop.htm> you may find information on Cochrane workshops throughout the world.

IN WANT OF CONSUMERS

The CHBG has yet not been successful in finding consumers. Should you be interested in what consumers do and need more information about their involvement, please visit the Cochrane Consumer Network's web page at
<http://www.cochraneconsumer.com/>, or contact us.

NOTE

The report on CHBG activities for 2000 and 2001 is prepared. Anybody wishing to get an electronic copy is welcome to require it by sending his/her email to <chbg@ctu.rh.dk> with a subject 'CHBG report required'. Those wishing paper copies are also requested to give us a note by e-mail or fax.

The Cochrane Hepato-Biliary (CHBG) Newsletter is prepared, edited, and published in electronic and paper format by staff at the CHBG Editorial Base in Copenhagen, Denmark. It is issued twice a year and distributed free of charge by The CHBG worldwide to all people on The CHBG list who either have contributed, are contributing, or show interest in the work of the Group. The purpose is to inform CHBG members and other interested parties about activities within The CHBG.

Editorial CHBG staff at the CHBG Editorial Base:

Christian Gluud, *Co-ordinating & Criticism Editor*, E-mail: <cgluud@ctu.rh.dk>;
Dimitrinka Nikolova, *Review Group Co-ordinator/Trials Search Co-ordinator*, E-mail: <dnikolov@ctu.rh.dk>;
Ninna Frydendal, *Assistant*, E-mail: <ninna.f@ctu.rh.dk>;
Nader Salasshahri, *IT advisor*, E-mail: <nader.s@ctu.rh.dk>

can be contacted by ordinary mail, phone, or fax.

Cochrane Hepato-Biliary Group,

Copenhagen Trial Unit,
Dept. 7102, H:S Rigshospitalet,
Blegdamsvej 9, DK-2100
Copenhagen Ø, Denmark,
Tel. +45 3545 7169 or +3545 7175,
Fax +45 3545 7101,
E-mail: <chbg@ctu.rh.dk >

Website: <<http://inet.uni2.dk/~ctucph/chbg>>