

EVIDENCE WORKSHEET

Guideline 14.1.2: GI cocktail for differentiating GERD/ACS in the ED

ANZCOR Subcommittee: ACS

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Clinical (PICO) question(s):

P: in patients with chest pain and suspected ACS,

I: does the use of a GI cocktail (oral viscous lidocaine/antacid/ +/- anticholinergic)

C: compared with standard diagnostic protocols (Serial ECG and biomarkers and provocative testing or imaging)

O: improve accuracy of diagnosis?

Search Strategies:

A. PUBMED

(Myocardial ischemia[mh] OR chest pain[mh] OR acute coronary syndrome[mh] OR myocardial infarction/di[mh] OR cardiac pain[ti] OR chest pain[ti] OR angina[ti] OR ACS[ti]) AND (Lidocaine/diagnostic use[mh] OR antacids[mh] OR Maalox[ti] OR donnatal[ti] OR Mylanta[ti] OR antacid[ti] OR antacid/anticholinergic[ti] OR antacid/alginate[ti] OR gaviscon[ti] OR topal[ti] OR xylocaine/diagnostic use[mh] OR GI cocktail[ti] OR pink lady[ti] OR white knight[ti])

Search results: 39

B. EMBASE

'thorax pain'/exp/mj OR 'heart infarction'/exp/mj OR 'angina pectoris'/exp/mj OR 'chest pain':ti OR infarction:ti OR 'acute coronary syndrome':ti OR angina:ti AND ('antacid agent'/exp/mj OR xylocaine:ti OR lignocaine:ti OR lidocaine:ti OR antacid:ti OR cocktail:ti OR 'pink lady':ti OR 'white knight':ti OR maalox:ti OR gaviscon:ti OR mylanta:ti OR donnatal:ti OR topal:ti) AND ('diagnosis'/exp/mj OR diagnosis:ab,ti OR diagnostic:ab,ti OR diagnose:ab,ti OR evaluate:ab,ti OR evaluation:ab,ti OR differentiate:ab,ti)

Search results: 84

C. COCHRANE CENTRAL

("chest pain" OR "myocardial infarction" OR "angina") AND ("antacid" OR "cocktail" OR "pink lady" OR "xylocaine" OR "lidocaine" OR "lignocaine") AND ("diagnosis" OR "diagnose" OR "diagnostic" OR "evaluate" OR "evaluation" OR "differentiate" OR "differentiation") in title abstract keywords in Trials'

Search results: 44

Additional studies identified through backward/forward searching: 3

Combined results: 181

After duplicates removed: 148

After inclusion/exclusion criteria applied: 14

Databases / other sources searched:

Grey literature, reference lists, Scopus

Inclusion criteria:

Clinical studies comparing the diagnostic accuracy of a GI cocktail (oral lidocaine/antacid +/- anticholinergic) with standard diagnostic protocol for the diagnosis of acute coronary syndrome in adult emergency department patients presenting with chest pain.

Exclusion criteria:

Non-comparative studies, non-human studies, studies where the full-text was not available in English, non-peer reviewed studies.

Search results:

The combined searches outlined above yielded 148 studies, which were assessed for inclusion as evidence.

Number of papers / studies meeting criteria for further review:

14 papers in the search after inclusion and exclusion

Methodological quality, levels of evidence & outcomes of studies examining the effect of family presence in resuscitation of adults:**Good**

The methodological quality of the study is high with the likelihood of any significant bias being minimal

Fair

The methodological quality of the study is reasonable with the potential for significant bias being likely.

Poor

The methodological quality of the study is weak possessing considerable and significant biases

1. Studies *supportive* of GI cocktail for ACS/GERD differentiation:

Friday 1977 is a letter to the editor that is opinion.

Schartz 1976 is a small number of patients enrolled in a single site registry. It studied the benefit of xylocaine/lignocaine in treating GERD type pain and differentiating such pain from ACS. No current standards for the exclusion of the diagnosis of ACS were applied. Probably the best supportive evidence.

Sixty patients with chest pain, chest and epigastric pain, or predominantly epigastric pain, not explained by electrocardiographic (EKG) changes or pulmonary findings, were given 20 cc of Xylocaine Viscous orally. Thirty-seven out of 60 experienced complete or almost complete relief within 10 to 15 minutes. Of this group, none were found to have suffered a myocardial infarction. Of the 23 patients who did not experience pain relief, six had a myocardial infarction and seven were diagnosed as having cardiac angina. Determination of serum lidocaine levels after oral ingestion of 20 cc of Xylocaine Viscous in patients with normal gastric function demonstrated a maximum level of 0.55 pg/ml -- a serum level unlikely to result in adverse side effects.

Good							
Fair							
Poor						Schwartz 1976	Friday 1977
	I	II	III-1	III-2	III-3	IV	Extrapolated evidence
NH&MRC levels of evidence							

2. Studies *neutral* for GI cocktail for ACS/GERD differentiation:

Bennett 1966 is a single centre observational registry. It is without current gold standards for the diagnosis of CAD .eg biomarkers and angiography. Does not study use of cocktail.

No Abstract Available

A prospective survey of all patients admitted to a general medical unit on account of precordial pain revealed that 23% had only alimentary-tract disease, mostly oesophagitis. The clinical features of oesophageal pain may closely resemble those of cardiac pain with identical radiation and precipitation by exercise or emotion. The investigation revealed the importance of oesophageal disease as a cause of precordial pain.

Berman 2003 (RCT Level II) of fair however is a study of Cocktail only in GERD and excludes pt with suspected Cardiac disease. It is no more effective than plain antacid in relieving symptoms in GERD.

Abstract—The “GI Cocktail” is a mixture of medications often given in the Emergency Department (ED) for

dyspepsia symptoms. Several combinations are used, but the most effective has not yet been determined. This study compared three combinations commonly given for dyspepsia. The study was a prospective, randomized, doubleblinded trial comparing antacid (group 1); antacid _ Donnatal _ (group 2); antacid _ Donnatal _ _ viscous lidocaine (group 3) for acute treatment of dyspepsia in the ED. Patients were randomly assigned to receive one of the three medication combinations. Patients rated their discomfort on a Visual Analog Scale (VAS) immediately before receiving the medication and 30 min later. Change in VAS was the primary study endpoint. A 13-mm difference in VAS was considered clinically significant. VAS change in the three groups was compared using multivariable regression, controlling for pretreatment VAS, study drug, previous antacid use, and gastrointestinal (GI) history. One hundred twenty patients were enrolled between July and December 2000. One hundred thirteen subjects (113) completed the protocol: Group 1 (N _ 38); Group 2 (N _ 37); Group 3 (N _ 38). There was no statistically significant difference between the groups in terms of age, gender, GI history, previous antacid use, or initial degree of pain. Group 1 had a 25 _ 27 mm mean (_ SD), decrease in pain; Group 2, 23 _ 22 mm decrease; and Group 3, 24 _ 26 mm decrease. There was no statistically significant difference in pain relief between the three groups on univariate analysis or multivariable regression. In conclusion, the addition of Donnatal_ or Donnatal_ _ lidocaine to an antacid did not relieve dyspepsia better than plain antacid. The “GI Cocktail” concoction may not be necessary.

Good							
Fair		Berman					

		2003					
Poor							Bennett 1966
	I	II	I I - 1	III-2	III-3	IV	Extrapolated evidence
NH&MRC levels of evidence							

3. Studies opposing GI cocktail for ACS/GERD differentiation:

Davies 1985 extrapolation that had shown that the instillation of acid into the stomach decreases the angina threshold on exercise testing.

The effect of oesophageal stimulation with acid on the exertional angina threshold was examined in 12 subjects. Each walked until the angina threshold was reached on four successive occasions; during two tests the oesophagus was instilled with 0.1 mol/l hydrochloric acid and during the other two with physiological saline. Oesophageal instillation was carried out for 20 min at rest before each walk. In 10 patients the angina point was reached after walking a significantly shorter distance on the treadmill when acid was instilled than when the saline was instilled. ST-segment changes and rate-pressure product were not significantly different during the acid and saline tests. The mechanism responsible for the reduction of angina threshold is not known. However, the effect was more pronounced in the 6 patients who had experienced regular oesophageal symptoms than in those who had not. Ischaemic heart disease and gastro-oesophageal reflux are both common, and the possibility that acid reflux may aggravate angina should be borne in mind, particularly when oesophageal symptoms are present.

Dickinson 1996 (case report) isolated cases report warning of the dangers of using cocktail to exclude ACS. No Abstract available.

Using a "GI Cocktail" in the emergency evaluation of chest pain is a diagnostic test for which the sensitivity and specificity are unknown. The case above illustrates how unreliable and potentially dangerous it can be. At the present time, the response of a patient with chest pain to a "GI Cocktail" has no place in the decision of whether to treat a patient's pain as cardiac, possibly cardiac, or noncardiac.

Goodacre 2003 from the ESCAPE trial (ps-RCT) does not study the use of cocktail but suggest the presence of indigestion type pain actually predicts ACS.

BACKGROUND: Patients with acute, undifferentiated chest pain present a frequent diagnostic challenge to clinicians. Clinical features are often used to determine which patients may have acute coronary syndrome (ACS).

AIM: To identify clinical features that independently predict ACS in patients with acute, undifferentiated chest pain.

DESIGN: Prospective study of patients enrolled in a randomized controlled trial.

METHODS: The presenting characteristics of participants in the ESCAPE randomized trial of chest pain

unit vs. routine care were recorded in a standardized manner.

Follow-up consisted of troponin T measurement at 2 days, postal questionnaire at 1 month, and telephone contact at 6 months. ACS was defined as elevated troponin T at 2 days or major adverse cardiac event within 30 days of presentation.

Multivariate analysis identified independent clinical predictors of ACS.

RESULTS: ACS was diagnosed in 77 (7.9%) of the 972 patients recruited. The following characteristics were independent predictors of ACS (odds ratio, p): age (1.09, $p < 0.001$), male gender (8.6, $p < 0.001$), indigestion or burning-type pain (3.0, $p = 0.034$), pain radiating to the left (2.4, $p = 0.013$) or right (5.7, $p < 0.001$) arm, vomiting (3.5, $p = 0.007$), and previous (5.1, $p < 0.001$) or current (3.7, $p < 0.001$) smoking.

DISCUSSION: In addition to previously recognized predictors of ACS, it appears that indigestion or burning type pain predicts ACS in patients attending the emergency department with acute, undifferentiated chest pain. Diagnosis of acute 'gastro-oesophageal' chest pain should be avoided in this setting.

Guda 2000 is published in abstract form and is a retrospective chart review in a relatively small number of patients.

Background: The GI Cocktail (Mylanta+ Lidocaine + Donnato) is a commonly used diagnostic tool in most emergency rooms (ER). Relief of dyspeptic symptoms including chest pain is considered diagnostic of gastritis or gastroesophageal reflux disease (GERD) as the etiology (Schwartz's test). *Aims:* Evaluate the diagnostic utility and therapeutic efficacy of GI Cocktail in the ER setting. *Design:* Chart review and telephonic interview for follow-up on outcome. *RESULTS:* Forty-four patients (28 females, 26 males, ages 5 to 89 years) who were given GI Cocktail at the ER were followed up after review of their initial charts. Twenty-four (54.5%) presented with abdominal pain, 12 (27%) with chest pain, 2 (4.5%) with chest wall pain, 6 (14%) with heartburn. Past medical history was significant for hypertension (20%), coronary artery disease (9%), and peptic ulcer disease (4.5%). Response to therapy was assessed by the ER physician based on clinical improvement of symptoms. Forty-one (93%) reported a good response within few minutes. Fifty seven percent of the patients, however, had received additional medications prior to assessment of the relief of pain. These included compazine 8 (18%), H2 blockers 5(11%), nitroglycerin 3 (7%), Tylenol 6(14%), no additional medications 9(20%). Irrespective of the relief of symptoms physicians proceeded to additional work up based on the history and clinical examination. 19 patients (43%) had electrocardiograms, 12 (27%) had cardiac enzymes checked. Of the patients presenting with abdominal pain 33% had electrocardiograms, 20% had cardiac enzymes done. Of those presenting with chest pain 92% had electrocardiograms and 50% had cardiac enzymes done. Two (4.5%) were hospitalized, one with suspected unstable coronary syndrome (EKG changes) and one secondary to a motor vehicle accident. When followed up, 41 (93%) had no recurrence of symptoms. None of these had to visit the ER second time during the follow up period. 52% had followed up with their primary physicians and 7% had ultrasonography.5 patients had further cardiac work up done. Only 2 (4.5%) were planned to have upper GI endoscopies. *CONCLUSION:* 1) There was no clearly demonstrable diagnostic utility of GI cocktail. 2) ER physicians often based their diagnostic work up depending on the patients clinical presentation, rather than the response to therapy. 3) It is difficult to establish a

clear benefit of this intervention since many of the patients had simultaneously received additional medications. 4) We believe that the relief of symptoms is most likely a placebo effect.

Henderson 1978 is a single centre registry describing the character of pain in GERD versus ACS. Relief of pain from antacids was not a reliable discriminator.

Cardiac and esophageal causes of atypical pain in the chest are often a difficult diagnostic problem. The pain is considered atypical because of its unusual distribution or unusual precipitating and relieving factors. One hundred and five patients with such pain were evaluated by complete esophageal and cardiac investigation. Based on the results of the investigations, 43 patients were found to have esophageal disease, 12 had cardiac disease, 21 had both cardiac and esophageal disease, and 29 had neither disorder. When the 43 patients with atypical esophageal disease were compared with 100 consecutive patients who had gastroesophageal reflux, it was found that in the patients with atypical esophageal disease, pain in the arm was more frequent, pain precipitated by exercise occurred frequently, and relief from pain with administration of antacids was less reliable. These factors accounted for the labelling of the disorder as atypical. Further difficulty in diagnosis was noted with the use of the technique of perfusion with acid. Although typical esophageal pain may be reproduced by such perfusion, all components of pain and, particularly, the distribution of pain to the arm cannot be reliably reproduced. Based on this study, we believed that in the patient with atypical pain in the chest, both cardiac and esophageal disease must be carefully evaluated if diagnostic errors are to be avoided.

Servi 1985 is a case series (3) demonstrating the dangers of using cocktail.

Simpson 1984 case series of 46 patients with proven MI showing though to be indigestion in 45% and relief symptoms in 29%.

Chest pain is a frequent presenting complaint in emergency departments. The etiology of chest pain is diverse; it can be evaluated with a history and physical examination, electrocardiogram, chest roentgenogram, or cardiac enzymes. When pathology in the upper gastrointestinal tract is suspected as the underlying source for chest discomfort, a gastrointestinal (GI) cocktail consisting of an antacid, an anticholinergic/ antispasmodic agent, and viscous xylocaine is often administered. Should the GI cocktail relieve the chest symptoms, the patient is discharged with the diagnosis of gastritis or esophagitis, which may not be correct. Several cases in which a GI cocktail completely relieved the pain of an evolving myocardial infarction are reported.

Teece 2003 Systematic review yielding two papers Henderson 1978 & Simpson 1984. Antacids are useful in the relief of pain that is clearly oesophageal in origin but the effect is insufficiently specific to be of value in aiding diagnosis.

A short cut review was carried out to establish whether antacids can be used as a diagnostic test in atypical chest pain. Altogether 374 papers were found using the reported search, of which two presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Wrenn 1995 A relatively small observational series concluding that there is little value from a GI cocktail as a diagnostic manoeuvre.

STUDY OBJECTIVE: To determine practice patterns regarding administration of the "GI cocktail" (a mixture of liquid antacid, viscous lidocaine, and an anticholinergic) in the emergency department in a single hospital and the responses and final dispositions of patients who received the cocktails. **DESIGN:** A retrospective review of ED charts. **SETTING:** Urban university hospital ED with an annual census of 50,000 visits. **PARTICIPANTS:** Ninety-seven consecutive patients who received a GI cocktail in the ED. **RESULTS:** Forty-nine patients (50%) received a GI cocktail for a chief complaint of abdominal pain and 40 (41%) for a chief complaint of chest pain. The reason for administration of a GI cocktail was documented on only one chart. Sixty-six patients (68%) received at least one other drug, at a median time of 9 minutes before administration of the GI cocktail. The most commonly coadministered drug was a narcotic (56 patients), followed by nitroglycerin (22 patients), antiemetics (13 patients), H2-blockers (13 patients), and aspirin (10 patients). Thirty-three patients (34%) had symptomatic relief with the cocktail alone, 35 (36%) had symptomatic relief with the cocktail plus other drugs, 7 (7%) had no response to the GI cocktail alone, and 5 (5%) had no response to the cocktail with other drugs. In 17 patients (18%) the response was not documented. Chest pain patients and abdominal pain patients had a similar frequency of response. There was also similarity of response between admitted and discharged patients. **CONCLUSION:** Although symptomatic relief after administration of a GI cocktail is often noted, it is difficult to differentiate the effects of the cocktail from those of other coadministered medications such as morphine or nitroglycerin. We urge ED physicians to use the GI cocktail in a rational manner.

Good							
Fair		Berman 2006					Goodacre 2003 Teece 2003 Davies 1985
Poor						Dickinson 1996 Guda 2000 Servi 1985 Wrenn 1995	Henderson 1978
	I	II	I I I - 1	III-2	III-3	IV	Extrapolated evidence
NH&MRC levels of evidence							

Endpoints:

Accuracy of diagnosis of ACS

Treatment recommendation:

In patients with chest pain and suspected ACS, the use of a GI cocktail (oral viscous lignocaine/antacid/ +/- anticholinergic) compared with standard diagnostic protocols (Serial ECG and biomarkers and provocative testing or imaging) is not proven to improve accuracy of diagnosis.

Reviewer's final comments and assessment of benefit / risk:

- Evidence is sparse and inconclusive.
- However a number of studies suggest harm in using antacid cocktail to improve the accuracy of diagnosis of ACS.

Citation List:

1-14

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