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[Intervention Review]

Emergency interventions for hyperkalaemia

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ABSTRACT

Background

Hyperkalaemia occurs in outpatients and in between 1% and 10% of hospitalised patients. When severe, consequences include arrhythmia and death.

Objectives

To review randomised evidence informing the emergency (i.e. acute, rather than chronic) management of hyperkalaemia

Search methods

We searched MEDLINE (1966-2003), EMBASE (1980-2003), *The Cochrane Library* (issue 4, 2003), and SciSearch using the text words hyperkal* or hyperpotass* (* indicates truncation). We also searched selected journals and abstracts of meetings. The reference lists of recent review articles, textbooks, and relevant papers were reviewed for additional potentially relevant titles.

Selection criteria

All selection was performed in duplicate. Articles were considered relevant if they were randomised, quasi-randomised or cross-over randomised studies of pharmacological or other interventions to treat non-neonatal humans with hyperkalaemia, reporting on clinically-important outcomes, or serum potassium levels within the first six hours of administration.

Data collection and analysis

All data extraction was performed in duplicate. We extracted quality information, and details of the patient population, intervention, baseline and follow-up potassium values. We extracted information about arrhythmias, mortality and adverse effects. Where possible, meta-analysis was performed using random effects models.

Main results

None of the studies of clinically-relevant hyperkalaemia reported mortality or cardiac arrhythmias. Reports focused on serum potassium levels. Many studies were small, and not all intervention groups had sufficient data for meta-analysis to be performed. On the basis of small studies, inhaled beta-agonists, nebulised beta-agonists, and intravenous (IV) insulin-and-glucose were all effective, and the combination of nebulised beta agonists with IV insulin-and-glucose was more effective than either alone. Dialysis is effective. Results were equivocal for IV bicarbonate. K-absorbing resin was not effective by four hours, and longer follow up data on this intervention were not available from RCTs.

Authors' conclusions

Nebulised or inhaled salbutamol, or IV insulin-and-glucose are the first-line therapies for the management of emergency hyperkalaemia that are best supported by the evidence. Their combination may be more effective than either alone, and should be considered when hyperkalaemia is severe. When arrhythmias are present, a wealth of anecdotal and animal data suggests that IV calcium is effective in treating arrhythmia. Further studies of the optimal use of combination treatments and of the adverse effects of treatments are needed.

PLAIN LANGUAGE SUMMARY

Emergency interventions for hyperkalaemia

No trials with clinically-important outcomes were identified. Many of the studies were conducted in convenience samples of patients. Many of the trials were methodologically flawed. Adverse events were rarely reported. Decrease in serum potassium was the most frequently reported outcome: for this outcome beta agonists and intravenous insulin-and-glucose were effective. The combination may be more effective than either alone.

BACKGROUND

Hyperkalaemia is defined as an excess concentration of potassium ions in the extracellular fluid compartment. Hyperkalaemia occurs in outpatients, and between 1% and 10% of hospitalised patients (Moore 1989; Paice 1983; Shemer 1983), often due to renal failure, hyperglycaemia, or inappropriate use of potassium supplements and other drugs that affect potassium homeostasis (Acker 1998; Moore 1989; Paice 1983; Shemer 1983). Commonly used therapies include intravenous (IV) calcium salts to reverse membrane polarization abnormalities (Greenberg 1998; Schwartz 1978; Weiner 1998); bicarbonate (Halperin 1998), insulin (Zierler 1987) or beta-2 agonists (Williams 1985) to shift potassium from the extracellular to the intracellular compartment; and resins (Berlyne 1966;Frohnert 1968; Johnson 1976 Scherr 1961) or dialysis (Blumberg 1988) to remove potassium from the extracellular compartment.

Patients with hyperkalaemia may experience weakness, fatigue, distal paraesthesiae, and respiratory depression (Freeman 1993). Changes in the electrocardiogram (ECG) include peaked T waves, QRS widening, and diminished P waves (Browning 1981). Severe hyperkalaemia can cause the QRS complex to merge with the T wave, leading to a sine wave pattern. This may progress to atrioventricular dissociation, ventricular tachycardia or fibrillation, and death.

Treatment for hyperkalaemia has been shown to vary from patient to patient within an institution, without obvious rationale (Acker 1998). Variations in recommendations for treatment of hyperkalaemia were observed in a survey of nephrology program directors (Iqbal 1989). No previous systematic review of this question has appeared.

OBJECTIVES

- To summarise randomised controlled trials (RCTs) and quasi-RCTs of acute interventions (calcium, insulin, beta-2 agonists, bicarbonate, ion-exchange resins and dialysis) in the treatment of patients with hyperkalaemia, with respect to the outcomes: serum potassium, ECG changes, arrhythmia, adverse effects of therapy and death.
- To identify whether the addition of beta-2 agonists to IV insulin is safe (few adverse effects) and effective (results in greater lowering of serum potassium than IV insulin alone).
- To identify whether the addition of IV insulin to beta-2 agonists is safe (few adverse effects) and effective (results in greater lowering of serum potassium than beta-2 agonists alone).
- To identify whether the addition of sodium bicarbonate to other agents of combinations is safe (few adverse effects) and effective (results in greater lowering of serum potassium than other agents or combinations alone).
- To identify areas in which further investigation is required.

METHODS

Criteria for considering studies for this review

Types of studies

RCTs, quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) and randomised cross-over studies were included.

Types of participants

Inclusion criteria

Non-neonatal (> one month old) humans (hyperkalaemia in neonates appears to be a distinct clinical problem and we did not wish to include studies of neonates).

Exclusion criteria

Artificially-induced hyperkalaemia.

Types of interventions

All interventions used in the emergency (acute, rather than chronic) treatment of hyperkalaemia were studied.
Pharmacological or other agents used to lower plasma (K+) or to treat or prevent adverse effects of hyperkalaemia.
Intervention was consistent between patients and described in sufficient detail to be reproducible.
At least one intervention given to five or more subjects.

Types of outcome measures

The following outcomes were of interest:

- plasma or serum potassium concentrations (pre-intervention and post-intervention),
- arrhythmias,
- ECG changes,
- adverse effects of interventions,
- death.

Outcomes within the first six hours of the intervention were studied.

Search methods for identification of studies

We searched the following databases:

- MEDLINE(1966-2003),
- EMBASE (1980-2003),
- *The Cochrane Library* (Issue 4, 2003)
- Cochrane Renal Group's specialised register of trials,
- SciSearch.

Articles were identified through the keyword search: hyperkal* OR hyperpotass*. In MEDLINE, the strategy was refined by combination (Boolean 'and') with an expert search strategy that has been shown to identify studies of therapeutic interventions with 98% sensitivity (Haynes 1994). We searched the journals *American College of Physicians Journal Club* and *Evidence Based Medicine* using the text words potassium, hyperkalemia/c and hyperkalaemia/c. Abstracts from the American Society of Nephrology meeting between 1996 and 2003 were searched using the same text words. We reviewed the reference lists of chapters describing the management of hyperkalemia in the following textbooks: Brenner and Rector's The Kidney (Brenner 2000), the Oxford Textbook of Nephrology (Davison 1998), Schrier's Diseases of the Kidney (Schrier 1993), and the online reference UpToDate. We also reviewed the reference lists of recent review articles on hyperkalaemia and all relevant studies. Studies were not excluded on the basis of language of publication.

Data collection and analysis

Thedatabase searching, identification of relevant articles, quality assessment and data extraction was performed independently in duplicate by two reviewers (BAM and WADS; DL and KT). Titles and abstracts were reviewed independently in duplicate and full text obtained for possibly relevant articles. Final decisions were made independently by the two reviewers on the basis of full text. Disagreements were resolved by group discussion including CMC, and consensus was reached in each case. Where data is available in text or tabulated form, this was extracted in preference to values displayed graphically. Where relevant outcomes (e.g. serum potassium) were reported only graphically, data were extracted from photographically enlarged copies of graphs. With the exception of data extracted from graphs, differences were resolved by consensus. For data extracted from graphs, the mean values of those obtained by each of the two reviewers were used, unless one set was clearly in error on comparison. Correspondence with study authors was attempted to complete missing data. Studies were not excluded on the basis of author, affiliation, language, journal or publication year. Final decisions to include or exclude based upon an examination of the full text of each identified article, along with additional information from authors who responded to questions.

Statistical assessment

Random effects models were used to combine outcomes for interventions versus placebo and for comparisons between interventions. If available, change in serum potassium from baseline to serum potassium 30 (± 5) minutes and 60 (± 5) minutes after the intervention were to be combined. Dichotomous outcomes (arrhythmia, death) were to be presented for the total follow-up period.

Subgroup analysis

We had prespecified a subgroup analysis summarising RCTs only (and excluding quasi-RCTs), however, no quasi-RCTs were identified. We had also planned to examine, if data permitted, whether effects were different in convenience samples (e.g. haemodialysis patients studied before a routine treatment), compared with patients requiring clinical treatment for hyperkalaemia; in end-stage renal disease (ESRD) patients compared with patients with renal function; in diabetics compared with nondiabetics; for route of administration of beta-2 agonists (IV versus nebulised versus aerosolised); and for hypertonic sodium bicarbonate compared with isotonic sodium bicarbonate. However, because of the small number of studies that provided data that could be combined, none of these subgroup analyses was possible.

Quality assessment

The methodological quality of each relevant study was characterised independently by two pairs of reviewers (BAM and WADS for studies before 1999; DL and KT for studies from 1999).

Studies were categorised as:

- RCTs,
- randomised crossover trials, or
- quasi-RCTs.

The following information was extracted:

- allocation concealment,
- blinding of participants, blinding of investigators, blinding of outcome assessment,
- intention-to-treat analysis,
- completeness of follow-up (> 80%).

We did not combine these quality items into a composite score. Studies were not excluded from the review on the basis of quality.

Heterogeneity

We planned to examine heterogeneity using Chi^2 and considering $P < 0.10$ as statistically significant, and the I^2 statistic (Higgins 2003).

Cross-over studies

We planned to use data from the time period prior to crossing over. However, we found none of the studies reported the two time periods separately, and we extracted the data as reported for all the patients.

Possible duplicate publications

When it appeared that there might be overlap in patient populations between two reports, we contacted authors to clarify the issue. If they did not respond, we used only data from the more recent publication.

RESULTS

Description of studies

From MEDLINE (1966-1998) the search strategy identified 282 citations, of which two relevant studies were identified by both reviewers (McClure 1994; Ngugi 1997). There were no disagreements (Kappa = 1.0). From the period of 1999 to 2003, 239 citations were identified in MEDLINE using the search strategy. These were reviewed in duplicate and two relevant articles were identified by each reviewer (Kappa = 1.0) (Mahajan 2001; Mandelberg 1999).

An EMBASE search from 1980 to 2003 identified 1234 articles. After deduplication against MEDLINE, two additional RCTs were identified by both reviewers (Kappa = 1.0) (Gruy-Kapral 1998; Pancu 2003). Cochrane search retrieved 219 articles. Nine relevant articles, six of which had not previously been identified in MEDLINE or EMBASE, were identified by both reviewers (Kappa = 1.0) (Allon 1989; Allon 1990; Allon 1995; Allon 1996; Gutzwiller 2003; Liou 1994). One of these articles excluded 'non-responders' from the analysis (Liou 1994). Data from this study are not considered further for this reason (a post-hoc exclusion). Kappa for this search was 0.94.

ACP Journal Club, Evidence-Based Medicine, the abstracts of the American Society of Nephrology, UpToDate, textbooks and review articles did not produce any additional studies that met the relevance criteria.

One other article was identified in the authors' files that was not identified by any of the search strategies (Zehnder 2001).

No studies reported the clinically-important outcomes of arrhythmia or death.

Most studies reported serum potassium levels at different time points after the initiation of the intervention. Most of the interventions studied had been examined in only one trial, and therefore combining data across studies was not possible. However, four studies comparing inhaled salbutamol (albuterol) with placebo were identified (Allon 1989; Allon 1996; Mandelberg 1999; Pancu 2003). Of these, one study compared two different doses (10 mg and 20 mg) of inhaled salbutamol with placebo (Allon 1989). We chose the data from the higher of the two doses for inclusion in the meta-analysis. A random effects model was used to combine outcomes for inhaled salbutamol versus placebo. The primary outcome was serum potassium at 30 minutes. Other time points as reported in the original papers have also been also shown.

In one of the studies of inhaled salbutamol included in the meta-analysis, standard deviations were given for the treatment group but not for the control group (Mandelberg 1999). In this case, the standard deviations for the control group were assumed to equal those of the control group at each time point. For a number of other comparisons, standard error of the means were given. In one case, neither standard error or standard deviations were given (Ngugi 1997). In this case, the missing standard deviations were entered as zeros and the data were not included in the pooled analyses.

Risk of bias in included studies

Twelve studies were included in this review. Eight were randomised crossover trials (Allon 1989; Allon 1990; Allon 1995; Allon 1996; Gruy-Kapral 1998; Gutzwiller 2003; McClure 1994; Zehnder 2001); four were RCTs with placebo (Pancu 2003; Mandelberg 1999) or without placebo (Mahajan 2001; McClure 1994; Ngugi 1997).

Allocation concealment was adequate in four studies (Allon 1989; Allon 1995; Allon 1996; Mandelberg 1999). The intervention was reproducibly described in all twelve studies. Three studies (Allon 1989; Mandelberg 1999; Pancu 2003) used blinding of investigators and patients to treatment. There was one single blinded study (Ngugi 1997). Cointerventions were not described in any study.

One study (Pancu 2003) reported either standard deviations or standard errors without stating which were used. Another study did not consistently report variances (Ngugi 1997). In some cases it was not explicitly stated whether standard error or standard deviation was reported for some or all of the values extracted. In these cases, we assumed that authors had used the same metric throughout, so that if standard errors were mentioned anywhere in the paper, the data were treated as standard errors in our analysis. In some papers, the standard deviation of absolute post-treatment values in the different groups were not reported. In these cases, we calculated the standard deviation of the absolute potassium value at each time point from the standard error of the difference, sample size per group, and standard deviation of the absolute value at baseline (Norman 1993).

Effects of interventions

None of the studies of clinically-relevant hyperkalaemia reported mortality or cardiac arrhythmias. Reports focussed on serum potassium levels. Characteristics are shown in the table of included studies. All appeared to be studies of convenience samples of patients with modest hyperkalaemia and either acute or chronic renal insufficiency. No study reported the emergency management of life-threatening hyperkalaemia. A number of studies did not report absolute values of serum potassium for time points later than baseline, or did not report variance in a usable way. Some papers reported change in potassium and standard error of the change, rather than the absolute values of potassium, and standard errors or standard deviations of the absolute values at different time points. These problems limited the number of studies from which combinable data could be extracted. For this reason, effect sizes and statistical significance for each individual study are described below, and are shown in the additional Table 1 - *Narrative summary of results for efficacy and harm*.

We contacted two authors in the hope of clarifying uncertainties or finding additional data, of whom one responded.

Beta-agonists

Eight studies (Allon 1989; Allon 1990; Allon 1995; Allon 1996; Mandelberg 1999; McClure 1994; Ngugi 1997; Pancu 2003) investigated the efficacy of beta-agonists in the treatment of hyperkalaemia (Analysis 1.1; Analysis 2.1; Analysis 3.1).

Inhaled or nebulised beta-agonists were effective, compared with placebo, by 30 minutes, and at all time points beyond that. Individual study results, not amenable to meta analysis, provided further information about dose-response, method of administration and time course of action (Allon 1989; Allon 1990; Allon 1995; Allon 1996; Mandelberg 1999; McClure 1994; Ngugi 1997; Pancu 2003). A dose-response relationship in maximum serum potassium reduction was observed: potassium values in the group receiving 20 mg nebulised salbutamol (albuterol) were lower than in the group receiving 10 mg throughout the experiment, reaching statistical significance ($P < 0.05$) at 120 minutes (Allon 1989). Compared with the placebo control, salbutamol (albuterol) and levalbuterol were equally effective in reducing serum potassium at 30 minutes and 60 minutes after drug introduction (Pancu 2003).

When comparing IV administration of salbutamol with nebulised salbutamol, no statistically significant differences were observed between groups. Based on the reporting of the variance estimates in this study, an effect estimate could not be calculated for this review (McClure 1994). For both routes of delivery, a second dose at 120 minutes caused further reductions in serum potassium (McClure 1994). Paradoxical elevation of serum potassium of 0.1 mmol/L or more was observed in 59% of patients one minute after administration of inhaled salbutamol (albuterol) in one study (Mandelberg 1999). In these patients, potassium returned to baseline by three minutes, and then fell progressively, reaching a statistically significant difference compared with placebo between five and 10 minutes.

No direct comparisons of the safety and efficacy of MDS-I with either nebulised or IV salbutamol were available.

Insulin in combination with glucose infusion

We were unable to perform meta-analysis for this intervention. However, four individual studies (Allon 1990; Allon 1996; Mahajan 2001; Ngugi 1997) investigated the efficacy of insulin with glucose in the treatment of emergency hyperkalaemia. Insulin with glucose was effective by 15 minutes in studies which assessed this time point (Allon 1990; Allon 1996), and at 30 minutes in all studies (Analysis 4.1; Analysis 14.1; Analysis 15.1; Analysis 16.1).

Resin potassium binders

One study (Gruy-Kapral 1998) addressed the effects of sodium polystyrene sulfonate on serum potassium in chronic renal failure patients. No differences in serum potassium were observed at four hours when resin was compared with placebo. No useful information on later time points could be extracted from this study, because oral potassium was administered at four hours (Analysis 5.1; Analysis 6.1; Analysis 7.1; Analysis 8.1).

Bicarbonate infusion

One study (Ngugi 1997) compared bicarbonate infusion with insulin and glucose and with salbutamol (albuterol) infusion, and found that it lowered serum potassium levels by 0.47 ± 0.31 mmol/L at 30 minutes (P = 0.001) and at all other time points. However in this study, the bicarbonate was less effective in reducing serum potassium than either of the alternatives (insulin, salbutamol). However, in the only placebo-controlled study (Allon 1996) bicarbonate therapy did not lower serum potassium at any time points out to 60 minutes (P = 0.60). Variance estimates for the absolute values were not available in either of these publications.

Dialysis

Two studies (Gutzwiller 2003; Zehnder 2001) investigated the utility of haemodialysis in serum potassium removal. The use of low-potassium (1 mmol/L and 2 mmol/L potassium chloride) and potassium-free dialysate was shown to be safe and effective in reducing serum potassium (Zehnder 2001). High potassium removal did not impair dialysis efficiency. There was a greater amount of potassium removed during dialysis with increasing blood flow (Gutzwiller 2003) (Analysis 10.1; Analysis 11.1; Analysis 12.1; Analysis 13.1).

Other

There were no placebo-controlled trials of aminophylline. In a comparison of aminophylline with IV insulin-glucose no significant difference was observed between groups (Mahajan 2001) (Analysis 16.1).

Combination of agents

One study (Allon 1990) showed that the addition of nebulised salbutamol to insulin and glucose is superior to either treatment alone at 30, 45 and 60 minutes, in the original between-group analysis of change in potassium concentration reported by the authors. This effect is not evident in our figure which, for consistency across studies, compares absolute potassium levels at different time points (Analysis 14.1).

One study (Ngugi 1997) compared a number of different combinations of agents with single agents. It was not possible to calculate effect sizes or compare groups since no estimates of variance were provided in this study. The authors did not specify the statistical procedures used, but concluded that there was no statistically significant difference between any of the treatment arms that they investigated (P = 0.794). Attempts to contact the authors for further information were unsuccessful. Allon 1995 found statistically significant differences in potassium levels when salbutamol used in combination with dialysis was compared with dialysis alone (Analysis 25.1).

The addition of IV bicarbonate to IV insulin or nebulised albuterol did not provide any greater lowering effect of serum potassium compared with either treatment alone (Allon 1996). Based on the reporting of the variance estimates in this study, an effect estimate could not be calculated for this review.

In addition to summary graphs in MetaView, the effect on serum potassium for individual study arms, categorised by intervention, are shown in addtional Figure 1; Figure 2; Figure 3; Figure 4; Figure 5; Figure 6; Figure 7; Figure 8; Figure 9; Figure 10; Figure 11).

Figure 1. Beta-agonist aerosolized

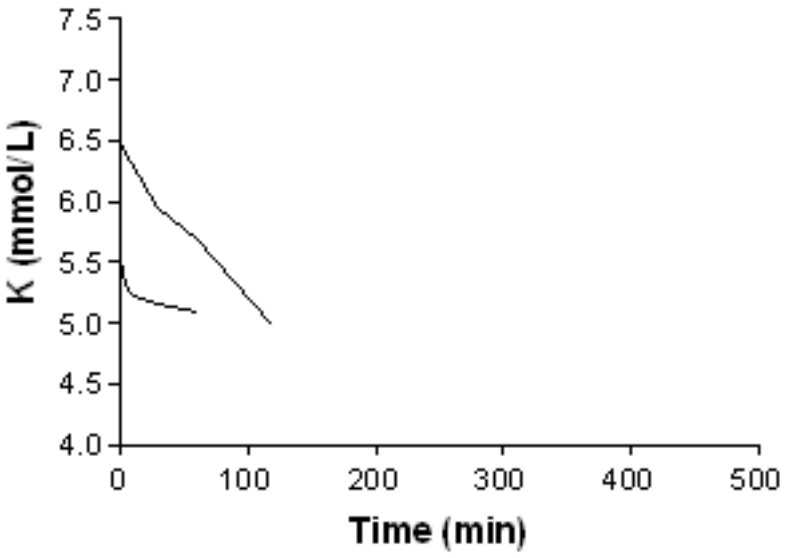


Figure 2. Beta-agonist aerosolized + insulin

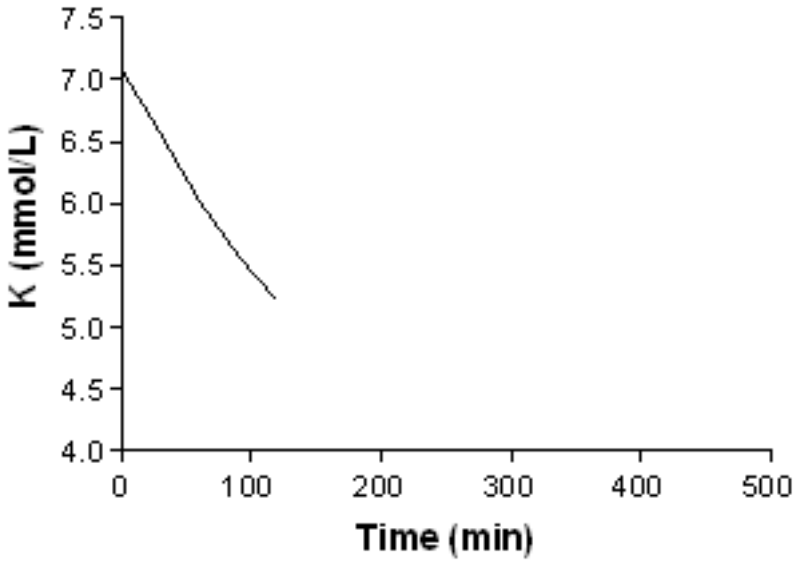


Figure 3. Beta-agonist IV

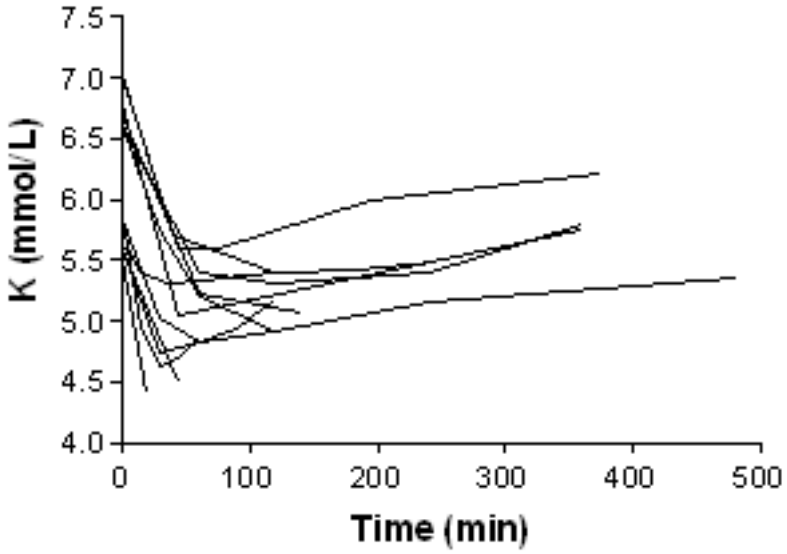


Figure 4. Beta-agonist + bicarbonate

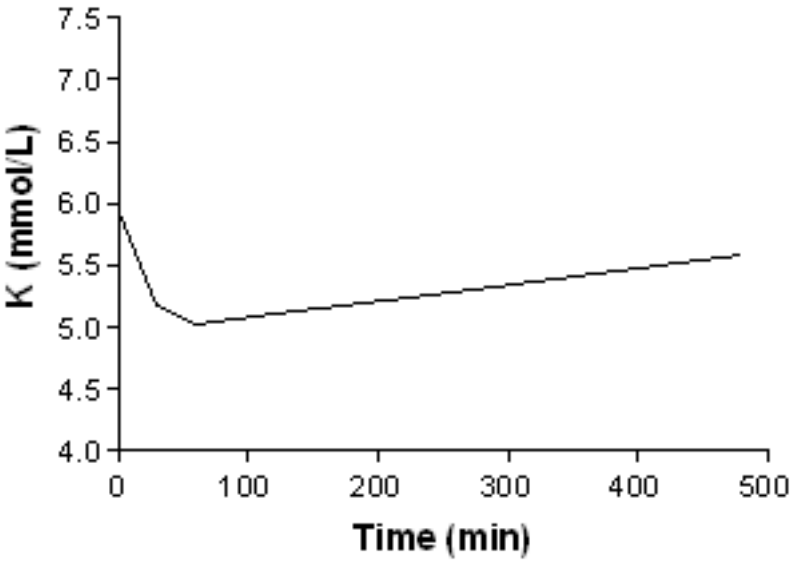


Figure 5. Beta-agonist nebulised

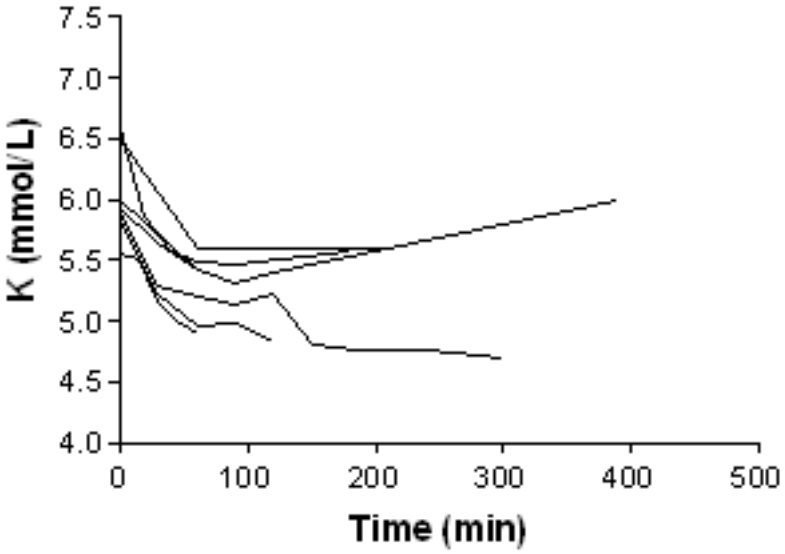


Figure 6. Beta-agonist nebulised + insulin

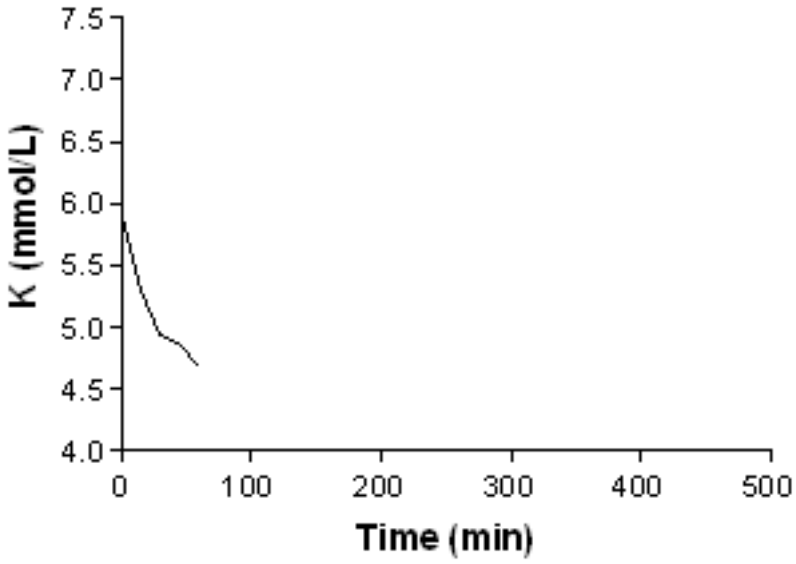


Figure 7. Beta agonist IV + insulin

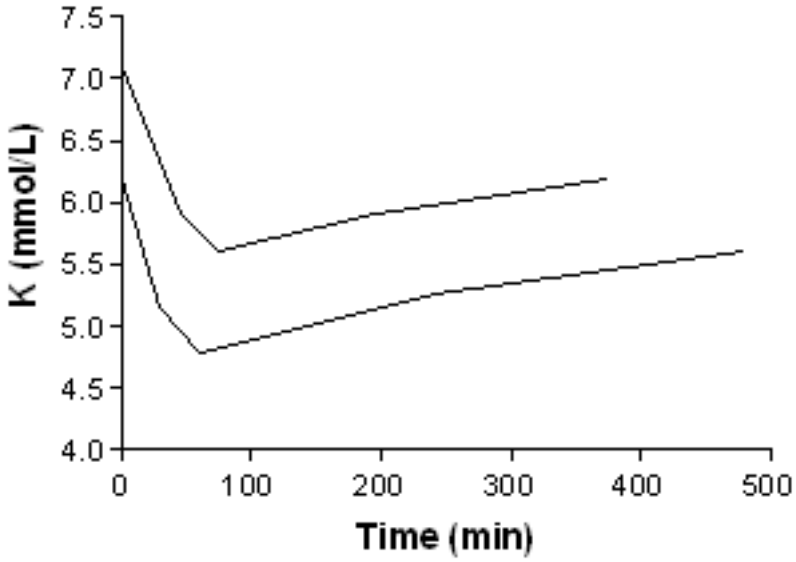


Figure 8. Beta-agonist Iv + insulin + bicarbonate

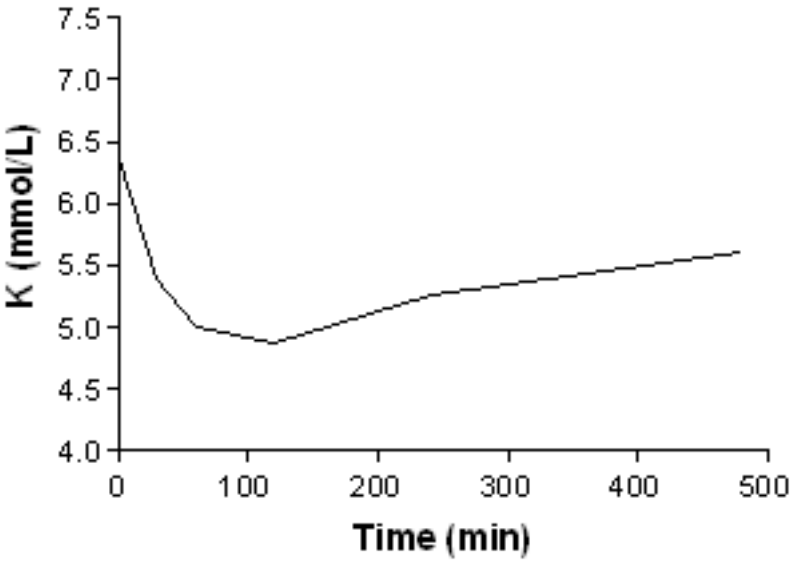


Figure 9. Bicarbonate

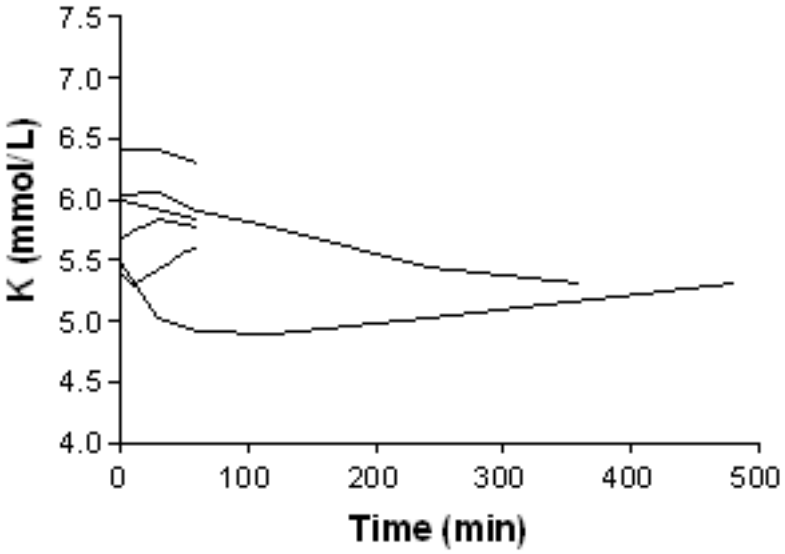


Figure 10. Insulin

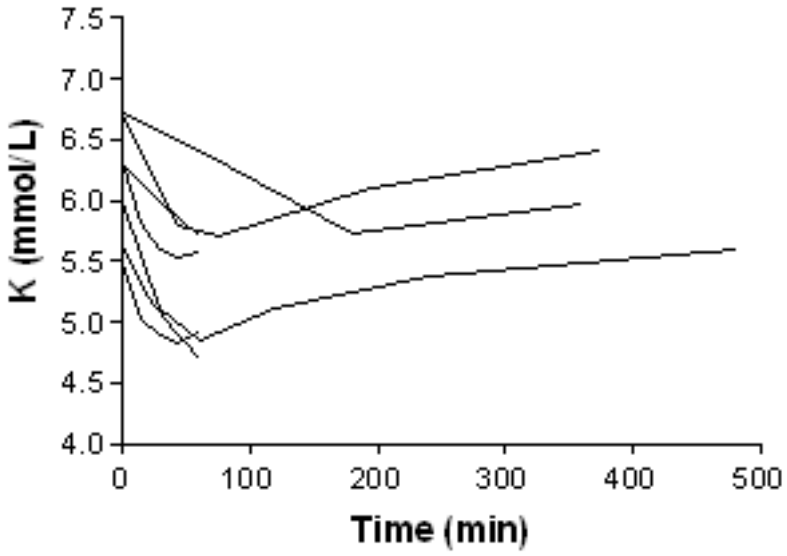
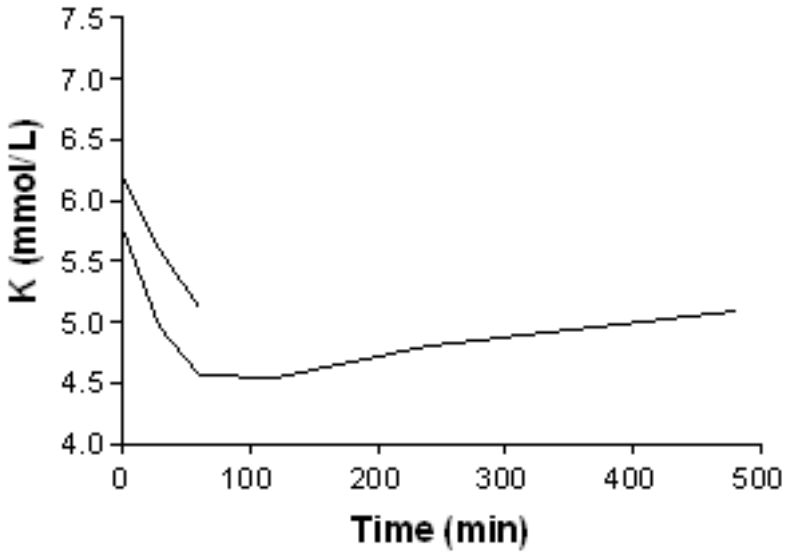


Figure 11. Insulin + bicarbonate



Adverse effects

Adverse effects are summarised in additional Table 1 - *Narrative summary of results for efficacy and harm*. No major adverse effects were reported with any intervention. Side effects with salbutamol (albuterol) included tremor, vasomotor flushing (McClure 1994) nervousness, palpitations, (Pancu 2003) mild anxiety (Allon 1989).and increases in heart rate (Allon 1990; Allon 1995; Mandelberg 1999; Pancu 2003). In one study (Pancu 2003), 4/9 patients had tachycardia with heart rates between 105 and 125 beats/minute. One patient, who had a previous history of paroxysmal atrial fibrillation, had an episode during treatment with salbutamol (albuterol). There was a single episode of hypoglycaemia with insulin use in one of the studies (Mahajan 2001). In Allon 1996 all three protocols that included bicarbonate therapy were associated with increases in serum bicarbonate (3.5 ± 0.5 mmol/L, 3.1 ± 0.5 mmol/L, 2.2 ± 0.5 mmol/L, $P < 0.005$) and pH (0.05 ± 0.01, 0.03 ± 0.01, 0.03 ± 0.01; $P < 0.01$).

DISCUSSION

The evidence

Because of the deleterious cardiac effects of hyperkalaemia, its management is an emergency intervention. We reviewed the evidence for various agents widely used for this problem. Heterogeneity in recommendations of experts in this scenario has been documented (Iqbal 1989) and is in keeping with the lack of clear evidence for the optimal regime.

There is evidence that the commonly practiced management options (salbutamol, insulin with glucose, dialysis) are effective. Salbutamol is effective when administered intravenously, nebulised, or as metered dose inhaler with spacer (MDS-I). While bicarbonate was found to be effective in one study (Ngugi 1997), it did not lower serum potassium below baseline in another (Allon 1996). Though resins are widely used clinically, there was no randomised evidence for their efficacy in an emergency setting, and one study showed no benefit (Gruy-Kapral 1998). Aminophylline, which is not commonly used in emergency management of hyperkalaemia, was found to be as effective as insulin and glucose, and safe. Combination of treatment modalities produced greater magnitudes of potassium lowering effect (Allon 1990; Allon 1995). One study (Allon 1996) found that when IV bicarbonate was added to salbutamol or to IV insulin-glucose therapy there was no additional benefit. Based on the reporting of variance estimates in this study, an effect estimate could not be calculated for this review.

No studies were identified which examined the role of increasing urine output (e.g. by fluid resuscitation, if appropriate; or by loop diuretics) to promote potassium excretion. Resins did not appear to be effective at four hours, though the dose of resin (30 g) used in the one study of this subject is lower than doses commonly used in clinical practice for the emergency management of hyperkalaemia. Since the site of action of resin is thought to be the colon, it is also possible that resins are not effective in the first few hours when given orally, but require longer to act. We are aware of two non-randomised studies that provided evidence of a potassium-lowering effect at 24 h exists for calcium resonium and sodium polystyrene sulphonate (Kayexalate) (Berlyne 1966; Scherr 1961). Dialysis with a low potassium bath (Zehnder 2001) and high blood flow rate (Gutzwiller 2003) was effective and safe.

No studies discussed the use of calcium salts given intravenously. The prevention of arrhythmia in the setting of hyperkalaemia was first observed by Ringer in 1883 (Ringer 1883) and corroborated by Winkler (Winkler 1939) and Thuillier (Thuillier 1952). Meroney (Meroney 1955) found IV calcium to be effective both in the treatment and prophylaxis of hyperkalaemia in humans. By the time of Chamberlain's classic review article on the emergency treatment of hyperkalaemia (Chamberlain 1964), the role of IV calcium in this setting appears to have been established.

Quality of the evidence

There were three double-blinded studies (Allon 1989; Mandelberg 1999; Pancu 2003). Allocation concealment was unclear in most of the studies. The sample sizes were small. Most studies did not comment on the number of participants completing the studies. In one study (Ngugi 1997), 90% of the patients completed the study period, the other 10% were started on dialysis before the end of the study period. Cointerventions were not explicitly described in any of the papers.

Publication bias

Given the small numbers of studies in each analysis we were not able to perform any analyses for publication bias. Publication bias may well exist in this literature, and would be expected to result in overestimating treatment effects.

Heterogeneity

Tests for heterogeneity are underpowered in analysis which include as few studies as are included in our analysis, and we do not think that much weight can be ascribed to the absence of statistically significant heterogeneity in our analyses.

Generalizability

Most of studies were in patients with ESRD which serves as a convenient model because patients are often mildly hyperkalaemic when due for dialysis. In addition, the absence of significant renal function simplifies the experiment, and increases generalizability to patients with reduced renal function, whether acute or chronic, in whom problems with hyperkalaemia are more likely. There is no good biological reason why treatment modalities that are effective in ESRD patients would not be applicable to the general population; however, it is possible that treatments that are ineffective or of equivocal effectiveness (e.g. IV bicarbonate) in patients with ESRD might still be effective in patients with normal renal function.

With the exception of dialysis, the treatment options are generally convenient, widely available, and feasible.

Limitations of current evidence

All the studies reported surrogate outcomes for efficacy, and not all commented on clinically-important adverse events. With the possible exception of Ngugi 1997, all studies appeared to have been conducted in convenience samples of mildly-hyperkalaemic individuals. Studies were in general small, and few comparisons of interventions were studied repeatedly. In many cases, standard deviations or standard errors were not reported numerically and were extracted from graphs. In one case, no variance estimates were reported. In other cases, whether error bars represented standard deviations or standard errors was not clearly reported and was inferred from data reported elsewhere in the same article. Statistical comparisons provided in the original article frequently reported changes from baseline and the statistical significance of this comparison, rather than the comparison between randomised groups. Very few data are available on the optimal combination of agents. No data were found on the role of IV calcium salts.

Limitations in this review

This review relied on authors' reporting on the quality of the study and the accuracy of the results. We did not contact all the authors for clarification or for original data, when the publication was unclear. We were unable to extract data from the first time period, before crossing over, from those studies which were cross over studies. This results in the inclusion of data that were not truly independent in the meta-analysis. We chose to leave these studies in the analysis because in each case we felt the wash-out period was adequate (usually 2-3 days) and because they represent a significant proportion of the available data.

Importance of review

We are not aware of any previous meta-analysis on this common medical problem. This review serves as a useful summary for clinicians and researchers.

AUTHORS' CONCLUSIONS

Implications for practice

The use of a beta-agonist appeared to be effective in rapid reduction of hyperkalaemia in both the setting of chronic renal failure adults and in children. Salbutamol is effective when given intravenously), in a nebulised form and as a multi-dose inhaler.

IV insulin and glucose is effective and has a rapid onset of action.

The evidence for the use of bicarbonate in hyperkalaemia is equivocal and we do not recommend its use as monotherapy. If used in conjunction with other treatments, the possible effects on pH and extracellular volume must be carefully considered in the assessment of the risk-benefit ratio for an individual patient.

Combining insulin-glucose with salbutamol (albuterol) probably leads to greater reductions in serum potassium than either alone.

Each of the treatments above relies on shifting potassium from extracellular to intracellular compartments in order to minimize its effects on the electrical stability of membranes. In animal and human studies, IV calcium stabilizes membranes and reduces the arrhythmic threshold. Though no randomised evidence exists to support its use, we recommend that calcium chloride (10 mL of 10%) be given in the presence of ECG changes or arrhythmia and repeated as needed. There is no randomised evidence that potassium-exchange resins are effective. In the absence of gastrointestinal pathology, these agents are safe, and may be instituted for their possible effects at 24 hours, but should not be relied upon for rapid effects. If medical therapy fails, or is deemed to be only a temporising measure because of concurrent renal failure, dialysis should be considered. Low-potassium and potassium-free dialysate (Zehnder 2001) and high blood flow (Gutzwiller 2003) are safe and effective in these circumstances.

Implications for research

The current body of evidence lacks large RCTs that are double-blinded, with clear allocation concealment. The dose-response relationship observed for salbutamol (albuterol) deserves further study, particularly with respect to optimising the reduction in serum potassium while minimizing adverse effects. The observation of additive benefits from the combination of insulin-glucose with salbutamol (albuterol) should be confirmed in a larger study. The evidence for bicarbonate is unclear, and well-designed randomized trials that address the effectiveness of isotonic and hypertonic bicarbonate when added nebulised salbutamol or to insulin and glucose are needed. A RCT of sodium polystyrene sulfonate (Kayexalate) and of calcium resonium, examining the time course of action of these agents would be of value.

Trials in patients with clinically-important hyperkalaemia, though difficult to conduct, could compare therapies known to be effective on the basis of studies of convenience samples, and collect information on clinically-important outcomes such as harm, arrhythmia and death.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Allon 1989

Methods	Prospective double-blind, placebo controlled study, outpatient haemodialysis clinic at a univeristy medical centre, paried student t-tests wtih bonferroni correction for repeated comparisons
Participants	10 Patients on maintenance haemodialysis who had chronic hyperkalaemia
Interventions	Nebulised albuterol therapy (10 mg or 20 mg) or placebo (saline)
Outcomes	Plasma potassium concentration, also serially measured blood pressure and pulse
Notes	Allocation concealment felt to be adequate only after clarification from author

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Allon 1990

Methods	Randomised prospective cross-over design, study conducted at the University of Oklahoma Health Sciences Center and Veterans Administration Medical Center
Participants	12 Nondiabetic hyperkalaemic patients on stable haemodialysis regiment
Interventions	a) regular insulin 10 units with glucose 50 mL of 50% solution IV over 5 minutes, b) nebulised treatment of albuterol 20 mg in 4 mL normal saline inhaled over 10 minute period, c) combined regimen consisting of intravenous insulin and dextrose as well as a nebulised albuterol treatment
Outcomes	Plasma potassium, Plasma glucose Plasma insulin
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Allon 1995

Methods	Randomised, prospective cross-over design
Participants	7 Patients on chronic haemodialysis
Interventions	Haemodialysis with nebulised albuterol 20 mg, 30 minutes Pre-dialysis versus haemodialysis only
Outcomes	Plasma potassium Glucose BUN Insulin
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Allon 1996

Methods	Randomised, prospective cross-over design, study conducted at the University of Alabama at Birmingham and the Veterans Administration Medical Center in Birmingham, ANOVA
Participants	8 Nondiabetic chronic haemodialysis patients
Interventions	There were 6 experimental protocols: 1. isotonic sodium bicarbonate at 90 mmol/h, 2. isotonic saline at 90 mmol/h, 3. isotonic bicarbonate (in 10% dextrose) at 90 mmol/h + IV insulin (5mU/kg/min), 4. isotonic saline (in 10% dextrose) at 90 mmol/h +IV insulin (5mU/kg/min), 5. isotonic bicarbonate at 90 mmol/h + nebulised albuterol (10 mg in 2.0 mL saline, nebulised over 10 minutes), and 6. isotonic saline at 90 mmol/h + nebulised albuterol (10mg in 2.0 mL saline, nebulised over 10 minutes)
Outcomes	Plasma potassium
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Gruy-Kapral 1998

Methods	Randomised controlled cross-over trial, 5 studies on 5 separate experimental days Study conducted in Dallas, Texas, USA, One way ANOVA and t-test
Participants	6 CRF patients on haemodialysis
Interventions	1). 8 gelatin capsules with 500 mL of water, versus 2). sodium polystyrene sulfonate (30 g of resin with 500 mL of water) versus 3). phenolphthalein-docusate (8 tablets with 500 mL of water) versus 4). phenolphthalein-docusate plus resin (8 tablets, 30 g of resin with 500 mL of water) versus 5). sorbitol plus resin (60 g of sorbitol, 30 g of resin with 500 mL of water)
Outcomes	Faecal potassium output Serum potassium concentration
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Gutzwiller 2003

Methods	Randomised, cross-over prospective study
Participants	13 ESRD patients on haemodialysis
Interventions	blood flows (Qb) of 200, 250, 300 mL/min, for 39 standardised high-flux haemodialysis treatments
Outcomes	Phosphate and potassium mass removal, Urea Phosphate Potassium
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Mahajan 2001

Methods	Randomised controlled trial Study conducted in India, Paired and unpaired student t-test

Mahajan 2001 *(Continued)*

Participants	30 ESRD patients admitted to Pt BD Sharma PGIMS Hospital
Interventions	Group A: aminophylline infusion Group B: insulin-dextrose infusion
Outcomes	Serum potassium Serum glucose
Notes	Aminophylline is a methylxanthine derivative Vitals monitored and ECG taken No serious side-effects observed

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Mandelberg 1999

Methods	Randomised double-blind placebo controlled cross-over trial conducted in Israel Fisher's exact, post-hoc t-test
Participants	17 CRF patients referred to Nehprology Unit between October 1, 1997 and March 31, 1998 for haemodialysis
Interventions	Group 1: 1200 ug salbutamol through MDS-I followed by placebo versus Group 2: placebo, then 1200 µg salbutamol through MDS-I
Outcomes	Serum potassium Insulin levels
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

McClure 1994

Methods	Randomised cross-over study, Study conducted in the United Kingdom
Participants	11 Children (aged 5-18 years) with end stage chronic renal failure
Interventions	Two doses of salbutamol (separated by two hours) given intravenously (4 µg/kg) and on a separate date, of salbutamol administered by nebuliser (2.5 mg if the child weighed below 25 kg, 5 mg if above) was observed

McClure 1994 *(Continued)*

Outcomes	Plasma potassium
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	D - Not used

Ngugi 1997

Methods	Randomised Controlled Trial, Study conducted in Nairobi
Participants	10 Patients with acute renal failure and 60 patients with chronic renal failure, both groups with hyperkalaemia
Interventions	Intervention A: Insulin 10U IV + 25 g glucose IV Intervention B: $NaCO_3$ 1 mmol/mL (8.4%) @ 3.3 mL/min x 15 min Intervention C: Albuterol 0.5 mL IV + 2.5 g glucose IV Intervention D: Interventions A + B Intervention E: Interventions B + C Intervention F: Interventions A + C Intervention G: Interventions A + B + C
Outcomes	Serum potassium
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Pancu 2003

Methods	Randomised double-blind placebo controlled trial Study conducted in USA, ANOVA across and within group
Participants	27 healthy volunteers, 9 subjects in each of the 3 study groups
Interventions	Nebulised albuterol 10 mg over 30 minutes versus Nebulised levalbuterol 2.5 mg over 30 minutes, versus Nornal saline in equivalent volumes
Outcomes	Serum potassium

Pancu 2003 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Zehnder 2001

Methods	Prospective randomised cross-over study
Participants	12 Non-diabetic haemodialysis patients
Interventions	Dialysates containing 0, 1, and 2 mmol/L of potassium
Outcomes	Mass removal of potassium and serum potassium
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Liou 1994	Non-responders of salbutamol excluded from the study

DATA AND ANALYSES

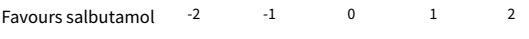
Comparison 1. Inhaled salbutamol versus placebo

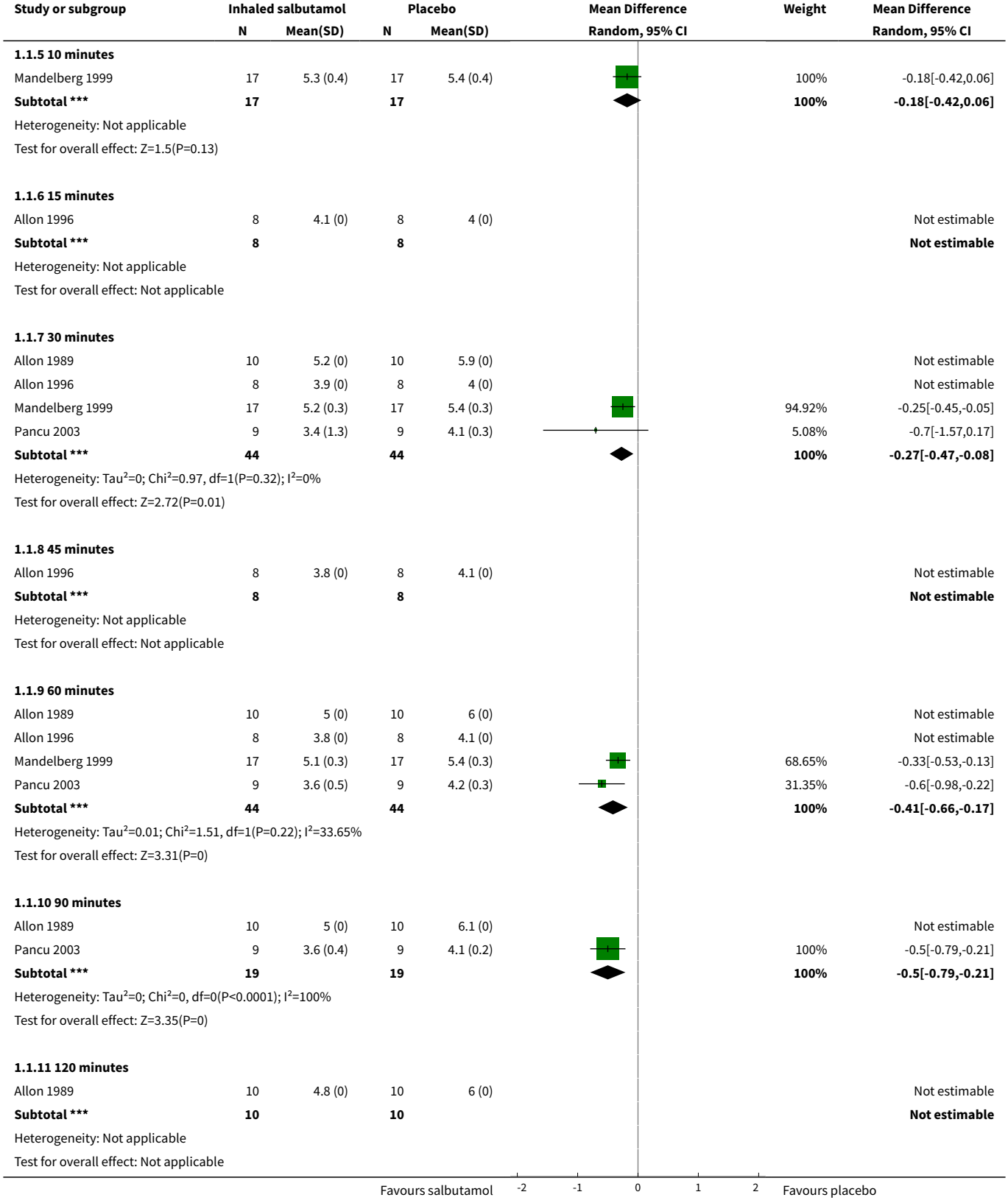
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 0 minutes	4	94	Mean Difference (IV, Random, 95% CI)	-0.00 [-0.19, 0.19]
1.2 1 minute	1	34	Mean Difference (IV, Random, 95% CI)	0.12 [-0.08, 0.32]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.3 3 minutes	1	34	Mean Difference (IV, Random, 95% CI)	0.0 [-0.24, 0.24]
1.4 5 minutes	1	34	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.34, 0.14]
1.5 10 minutes	1	34	Mean Difference (IV, Random, 95% CI)	-0.18 [-0.42, 0.06]
1.6 15 minutes	1	16	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.7 30 minutes	4	88	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.47, -0.08]
1.8 45 minutes	1	16	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.9 60 minutes	4	88	Mean Difference (IV, Random, 95% CI)	-0.41 [-0.66, -0.17]
1.10 90 minutes	2	38	Mean Difference (IV, Random, 95% CI)	-0.50 [-0.79, -0.21]
1.11 120 minutes	1	20	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Inhaled salbutamol versus placebo, Outcome 1 Serum potassium.

Study or subgroup	Inhaled salbutamol N	Inhaled salbutamol Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 0 minutes							
Allon 1989	10	5.8 (1.3)	10	5.7 (0.8)		3.83%	0.07[-0.86,1]
Allon 1996	8	4.3 (0.3)	8	4.1 (0.3)		27.25%	0.17[-0.14,0.48]
Mandelberg 1999	17	5.5 (0.4)	17	5.4 (0.4)		32.61%	0.07[-0.2,0.34]
Pancu 2003	9	3.9 (0.3)	15	4.1 (0.3)		36.31%	-0.2[-0.45,0.05]
Subtotal ***	**44**		**50**			**100%**	**-0[-0.19,0.19]**
Heterogeneity: Tau^2=0.01; Chi^2=3.96, df=3(P=0.27); I^2=24.25%							
Test for overall effect: Z=0.01(P=0.99)							
1.1.2 1 minute							
Mandelberg 1999	17	5.6 (0.3)	17	5.4 (0.3)		100%	0.12[-0.08,0.32]
Subtotal ***	**17**		**17**			**100%**	**0.12[-0.08,0.32]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.17(P=0.24)							
1.1.3 3 minutes							
Mandelberg 1999	17	5.4 (0.4)	17	5.4 (0.4)		100%	0[-0.24,0.24]
Subtotal ***	**17**		**17**			**100%**	**0[-0.24,0.24]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.1.4 5 minutes							
Mandelberg 1999	17	5.3 (0.4)	17	5.4 (0.4)		100%	-0.1[-0.34,0.14]
Subtotal ***	**17**		**17**			**100%**	**-0.1[-0.34,0.14]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.83(P=0.4)							





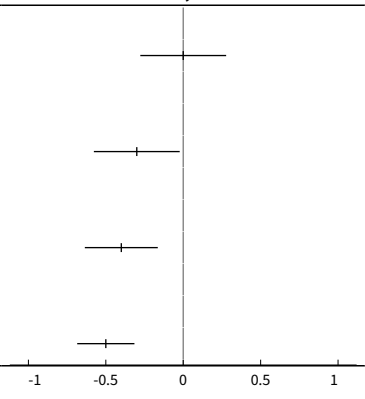
Study or subgroup	Inhaled salbutamol N	Inhaled salbutamol Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.5 10 minutes							
Mandelberg 1999	17	5.3 (0.4)	17	5.4 (0.4)		100%	-0.18[-0.42,0.06]
Subtotal ***	**17**		**17**			**100%**	**-0.18[-0.42,0.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.5(P=0.13)							
1.1.6 15 minutes							
Allon 1996	8	4.1 (0)	8	4 (0)			Not estimable
Subtotal ***	**8**		**8**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.1.7 30 minutes							
Allon 1989	10	5.2 (0)	10	5.9 (0)			Not estimable
Allon 1996	8	3.9 (0)	8	4 (0)			Not estimable
Mandelberg 1999	17	5.2 (0.3)	17	5.4 (0.3)		94.92%	-0.25[-0.45,-0.05]
Pancu 2003	9	3.4 (1.3)	9	4.1 (0.3)		5.08%	-0.7[-1.57,0.17]
Subtotal ***	**44**		**44**			**100%**	**-0.27[-0.47,-0.08]**
Heterogeneity: Tau^2=0; Chi^2=0.97, df=1(P=0.32); I^2=0%							
Test for overall effect: Z=2.72(P=0.01)							
1.1.8 45 minutes							
Allon 1996	8	3.8 (0)	8	4.1 (0)			Not estimable
Subtotal ***	**8**		**8**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.1.9 60 minutes							
Allon 1989	10	5 (0)	10	6 (0)			Not estimable
Allon 1996	8	3.8 (0)	8	4.1 (0)			Not estimable
Mandelberg 1999	17	5.1 (0.3)	17	5.4 (0.3)		68.65%	-0.33[-0.53,-0.13]
Pancu 2003	9	3.6 (0.5)	9	4.2 (0.3)		31.35%	-0.6[-0.98,-0.22]
Subtotal ***	**44**		**44**			**100%**	**-0.41[-0.66,-0.17]**
Heterogeneity: Tau^2=0.01; Chi^2=1.51, df=1(P=0.22); I^2=33.65%							
Test for overall effect: Z=3.31(P=0)							
1.1.10 90 minutes							
Allon 1989	10	5 (0)	10	6.1 (0)			Not estimable
Pancu 2003	9	3.6 (0.4)	9	4.1 (0.2)		100%	-0.5[-0.79,-0.21]
Subtotal ***	**19**		**19**			**100%**	**-0.5[-0.79,-0.21]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=3.35(P=0)							
1.1.11 120 minutes							
Allon 1989	10	4.8 (0)	10	6 (0)			Not estimable
Subtotal ***	**10**		**10**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

Comparison 2. Nebulised levalbuterol 2.5 mg versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes/immediate post-treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 60 minutes/30 minutes post-treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 90 minutes/60 minutes post-treatment	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Nebulised levalbuterol 2.5 mg versus placebo, Outcome 1 Serum potassium.

Study or subgroup	Levalbuterol N	Levalbuterol Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
2.1.1 0 minutes						
Pancu 2003	9	4.1 (0.3)	9	4.1 (0.3)		0[-0.28,0.28]
2.1.2 30 minutes/immediate post-treatment						
Pancu 2003	9	3.8 (0.3)	9	4.1 (0.3)		-0.3[-0.58,-0.02]
2.1.3 60 minutes/30 minutes post-treatment						
Pancu 2003	9	3.8 (0.2)	9	4.2 (0.3)		-0.4[-0.64,-0.16]
2.1.4 90 minutes/60 minutes post-treatment						
Pancu 2003	9	3.6 (0.2)	9	4.1 (0.2)		-0.5[-0.68,-0.32]



Comparison 3. IV salbutamol versus nebulised salbutamol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 90 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.5 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 150 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.7 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.8 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.9 300 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 3.1. Comparison 3 IV salbutamol versus nebulised salbutamol, Outcome 1 Serum potassium.

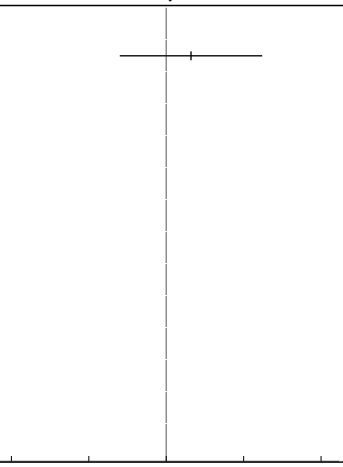
Study or subgroup	IV salbutamol		Nebulised salbutamol		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
3.1.1 0 minutes						
McClure 1994	10	5.6 (0)	10	5.9 (0)		Not estimable
3.1.2 30 minutes						
McClure 1994	10	4.7 (0)	10	5.3 (0)		Not estimable
3.1.3 60 minutes						
McClure 1994	10	4.8 (0)	10	5.2 (0)		Not estimable
3.1.4 90 minutes						
McClure 1994	10	4.9 (0)	10	5.1 (0)		Not estimable
3.1.5 120 minutes						
McClure 1994	10	5.2 (0)	10	5.2 (0)		Not estimable
3.1.6 150 minutes						
McClure 1994	10	4.4 (0)	10	4.8 (0)		Not estimable
3.1.7 180 minutes						
McClure 1994	10	4.5 (0)	10	4.8 (0)		Not estimable
3.1.8 240 minutes						
McClure 1994	10	4.8 (0)	10	4.8 (0)		Not estimable
3.1.9 300 minutes						
McClure 1994	10	4.7 (0)	10	4.8 (0)		Not estimable

Comparison 4. IV insulin-glucose versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 4.1. Comparison 4 IV insulin-glucose versus placebo, Outcome 1 Serum potassium.

Study or subgroup	IV insulin-glucose N	IV insulin-glucose Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
4.1.1 0 minutes						
Allon 1996	8	4.3 (0.6)	8	4.1 (0.3)		0.16[-0.3,0.62]
4.1.2 15 minutes						
Allon 1996	8	3.8 (0)	8	4 (0)		Not estimable
4.1.3 30 minutes						
Allon 1996	8	3.6 (0)	8	4 (0)		Not estimable
4.1.4 45 minutes						
Allon 1996	8	3.5 (0)	8	4.1 (0)		Not estimable
4.1.5 60 minutes						
Allon 1996	8	3.4 (0)	8	4.1 (0)		Not estimable

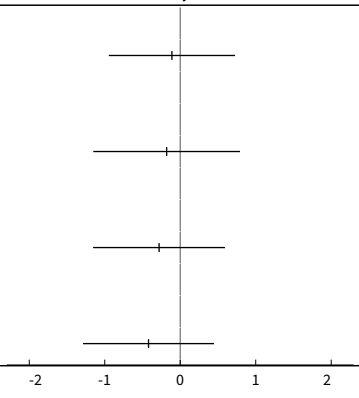


Comparison 5. Sodium polystyrene sulphonate versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 720 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 5.1. Comparison 5 Sodium polystyrene sulphonate versus placebo, Outcome 1 Serum potassium.

Study or subgroup	Resin		placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
5.1.1 0 minutes						
Gruy-Kapral 1998	6	4.2 (0.7)	6	4.3 (0.8)		-0.11[-0.95,0.73]
5.1.2 240 minutes						
Gruy-Kapral 1998	6	4.3 (0.6)	6	4.4 (1.1)		-0.18[-1.15,0.79]
5.1.3 480 minutes						
Gruy-Kapral 1998	6	4.3 (0.7)	6	4.6 (0.8)		-0.28[-1.15,0.59]
5.1.4 720 minutes						
Gruy-Kapral 1998	6	4.3 (0.7)	6	4.7 (0.9)		-0.42[-1.29,0.45]



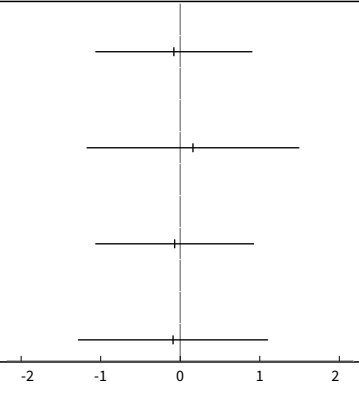
Favours resin — Favours placebo

Comparison 6. Phenolphthalein-docusate versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 720 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 6.1. Comparison 6 Phenolphthalein-docusate versus placebo, Outcome 1 Serum potassium.

Study or subgroup	Phenolph-thalein-dosusate		Placebo		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
6.1.1 0 minutes						
Gruy-Kapral 1998	6	4.2 (0.9)	6	4.3 (0.8)		-0.08[-1.07,0.91]
6.1.2 240 minutes						
Gruy-Kapral 1998	6	4.6 (1.3)	6	4.4 (1.1)		0.16[-1.18,1.5]
6.1.3 480 minutes						
Gruy-Kapral 1998	6	4.5 (0.9)	6	4.6 (0.8)		-0.07[-1.07,0.93]
6.1.4 720 minutes						
Gruy-Kapral 1998	6	4.6 (1.2)	6	4.7 (0.9)		-0.09[-1.28,1.1]



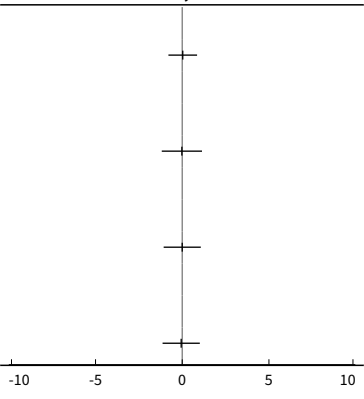
Favours phenolphthalein-dosusate — Favours placebo

Comparison 7. Phenolphthalein-docusate plus sodium polystyrene sulphonate versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 720 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 7.1. Comparison 7 Phenolphthalein-docusate plus sodium polystyrene sulphonate versus placebo, Outcome 1 Serum potassium.

Study or subgroup	Phenolphthalein + resin N	Phenolphthalein + resin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
7.1.1 0 minutes						
Gruy-Kapral 1998	6	4.4 (0.6)	6	4.3 (0.8)		0.03[-0.8,0.86]
7.1.2 240 minutes						
Gruy-Kapral 1998	6	4.4 (1)	6	4.4 (1.1)		-0.02[-1.18,1.14]
7.1.3 480 minutes						
Gruy-Kapral 1998	6	4.6 (1.1)	6	4.6 (0.8)		0[-1.07,1.07]
7.1.4 720 minutes						
Gruy-Kapral 1998	6	4.7 (1)	6	4.7 (0.9)		-0.06[-1.13,1.01]

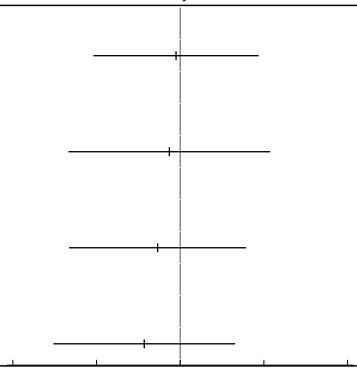


Comparison 8. Sorbitol plus sodium polystyrene sulphonate versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 720 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 8.1. Comparison 8 Sorbitol plus sodium polystyrene sulphonate versus placebo, Outcome 1 Serum potassium.

Study or subgroup	Sorbitol + resin N	Sorbitol + resin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
8.1.1 0 minutes						
Gruy-Kapral 1998	6	4.3 (0.9)	6	4.3 (0.8)		-0.05[-1.04,0.94]
8.1.2 240 minutes						
Gruy-Kapral 1998	6	4.3 (1.1)	6	4.4 (1.1)		-0.13[-1.34,1.08]
8.1.3 480 minutes						
Gruy-Kapral 1998	6	4.3 (1)	6	4.6 (0.8)		-0.27[-1.33,0.79]
8.1.4 720 minutes						
Gruy-Kapral 1998	6	4.3 (1.1)	6	4.7 (0.9)		-0.43[-1.52,0.66]

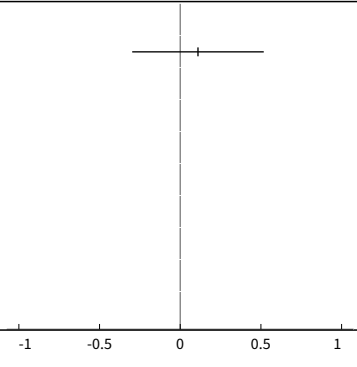


Comparison 9. IV bicarbonate versus placebo

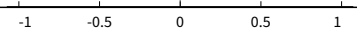
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 9.1. Comparison 9 IV bicarbonate versus placebo, Outcome 1 Serum potassium.

Study or subgroup	IV bicarbonate N	IV bicarbonate Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
9.1.1 0 minutes						
Allon 1996	8	4.2 (0.5)	8	4.1 (0.3)		0.11[-0.3,0.52]
9.1.2 15 minutes						
Allon 1996	8	4.2 (0)	8	4 (0)		Not estimable
9.1.3 30 minutes						
Allon 1996	8	4.1 (0)	8	4 (0)		Not estimable
9.1.4 45 minutes						



Study or subgroup	IV bicarbonate N	IV bicarbonate Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Allon 1996	8	4.2 (0)	8	4.1 (0)		Not estimable
9.1.5 60 minutes						
Allon 1996	8	4.2 (0)	8	4.1 (0)		Not estimable



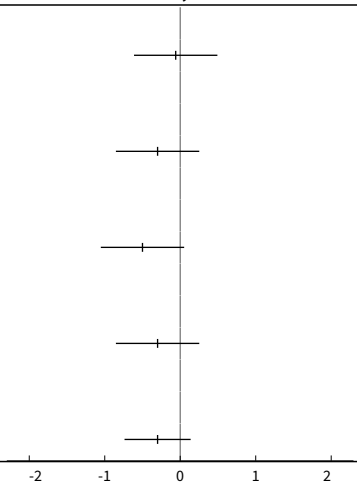
Favours IV bicarbonate — Favours placebo

Comparison 10. Haemodialysis: 0K dialysate versus 1K dialysate

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 10.1. Comparison 10 Haemodialysis: 0K dialysate versus 1K dialysate, Outcome 1 Serum potassium.

Study or subgroup	0K dialysate N	0K dialysate Mean(SD)	1K dialysate N	1K dialysate Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
10.1.1 0 minutes						
Zehnder 2001	12	4.4 (0.7)	12	4.5 (0.7)		-0.06[-0.61,0.49]
10.1.2 60 minutes						
Zehnder 2001	12	3.2 (0.7)	12	3.5 (0.7)		-0.3[-0.85,0.25]
10.1.3 120 minutes						
Zehnder 2001	12	2.9 (0.7)	12	3.4 (0.7)		-0.5[-1.05,0.05]
10.1.4 180 minutes						
Zehnder 2001	12	2.8 (0.7)	12	3.1 (0.7)		-0.3[-0.85,0.25]
10.1.5 240 minutes						
Zehnder 2001	12	2.7 (0.4)	12	3 (0.7)		-0.3[-0.74,0.14]



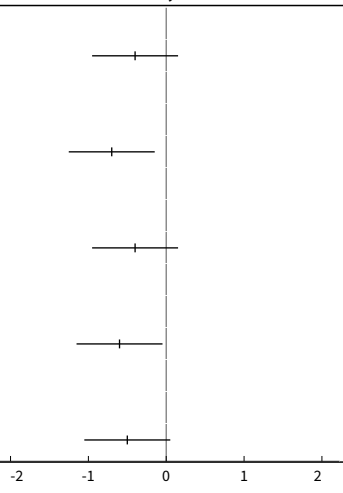
Favours 0K dialysate — Favours 1K dialysate

Comparison 11. Haemodialysis: 1K dialysate versus 2K dialysate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 11.1. Comparison 11 Haemodialysis: 1K dialysate versus 2K dialysate, Outcome 1 Serum potassium.

Study or subgroup	1K dialysate N	1K dialysate Mean(SD)	2K dialysate N	2K dialysate Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
11.1.1 0 minutes						
Zehnder 2001	12	4.5 (0.7)	12	4.9 (0.7)		-0.4[-0.95,0.15]
11.1.2 60 minutes						
Zehnder 2001	12	3.5 (0.7)	12	4.2 (0.7)		-0.7[-1.25,-0.15]
11.1.3 120 minutes						
Zehnder 2001	12	3.4 (0.7)	12	3.8 (0.7)		-0.4[-0.95,0.15]
11.1.4 180 minutes						
Zehnder 2001	12	3.1 (0.7)	12	3.7 (0.7)		-0.6[-1.15,-0.05]
11.1.5 240 minutes						
Zehnder 2001	12	3 (0.7)	12	3.5 (0.7)		-0.5[-1.05,0.05]



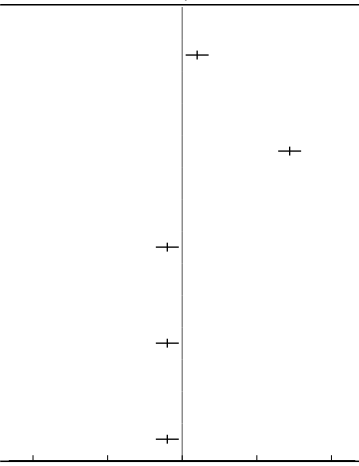
Comparison 12. High flux haemodialysis: blood flow 300 mL/min versus 250 mL/min

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 12.1. Comparison 12 High flux haemodialysis: blood flow 300 mL/min versus 250 mL/min, Outcome 1 Serum potassium.

Study or subgroup	300 mL/min N	300 mL/min Mean(SD)	250 mL/min N	250 mL/min Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
12.1.1 0 minutes						
Gutzwiller 2003	13	4.6 (0.1)	13	4.5 (0.1)		0.1[0.02,0.18]
12.1.2 60 minutes						
Gutzwiller 2003	13	3.8 (0.1)	13	3.1 (0.1)		0.72[0.64,0.8]
12.1.3 120 minutes						
Gutzwiller 2003	13	3.6 (0.1)	13	3.7 (0.1)		-0.1[-0.18,-0.02]
12.1.4 180 minutes						
Gutzwiller 2003	13	3.5 (0.1)	13	3.6 (0.1)		-0.1[-0.18,-0.02]
12.1.5 240 minutes						
Gutzwiller 2003	13	3.5 (0.1)	13	3.6 (0.1)		-0.1[-0.18,-0.02]

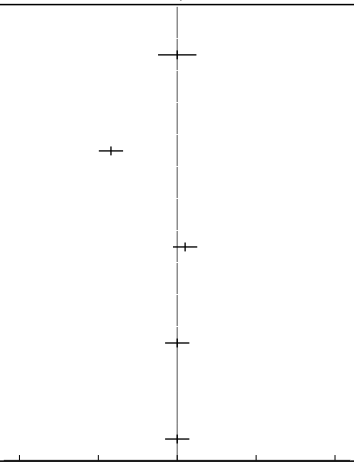


Comparison 13. High flux haemodialysis: blood flow 250 mL/min versus 200 mL/min

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 13.1. Comparison 13 High flux haemodialysis: blood flow 250 mL/min versus 200 mL/min, Outcome 1 Serum potassium.

Study or subgroup	250 mL/min N	250 mL/min Mean(SD)	200 mL/min N	200 mL/min Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
13.1.1 0 minutes						
Gutzwiller 2003	13	4.5 (0.2)	13	4.5 (0.1)		0[-0.12,0.12]
13.1.2 60 minutes						
Gutzwiller 2003	13	3.4 (0.1)	13	3.8 (0.1)		-0.42[-0.5,-0.34]
13.1.3 120 minutes						
Gutzwiller 2003	13	3.8 (0.1)	13	3.7 (0.1)		0.05[-0.03,0.13]
13.1.4 180 minutes						
Gutzwiller 2003	13	3.6 (0.1)	13	3.6 (0.1)		0[-0.08,0.08]
13.1.5 240 minutes						
Gutzwiller 2003	13	3.6 (0.1)	13	3.6 (0.1)		0[-0.08,0.08]

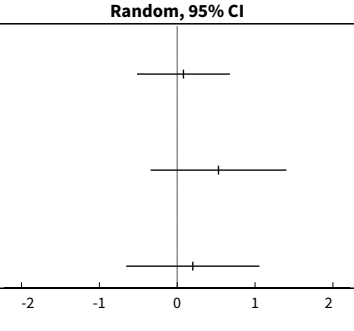


Comparison 14. Nebulised salbutamol versus IV insulin-glucose

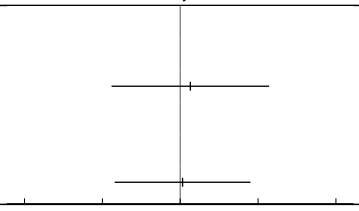
Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 14.1. Comparison 14 Nebulised salbutamol versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	Salbutamol N	Salbutamol Mean(SD)	Insulin-glucose N	Insulin-glucose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.1.1 0 minutes						
Allon 1990	12	5.6 (0.8)	12	5.5 (0.7)		0.08[-0.52,0.68]
14.1.2 15 minutes						
Allon 1990	12	5.5 (1.1)	12	5 (1.1)		0.53[-0.34,1.4]
14.1.3 30 minutes						
Allon 1990	12	5.1 (1.1)	12	4.9 (1.1)		0.2[-0.66,1.06]



Study or subgroup	Salbutamol N	Salbutamol Mean(SD)	Insulin-glucose N	Insulin-glucose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
14.1.4 45 minutes						
Allon 1990	12	5 (1.3)	12	4.8 (1.3)		0.13[-0.88,1.14]
14.1.5 60 minutes						
Allon 1990	12	4.9 (1.1)	12	4.9 (1.1)		0.03[-0.84,0.9]

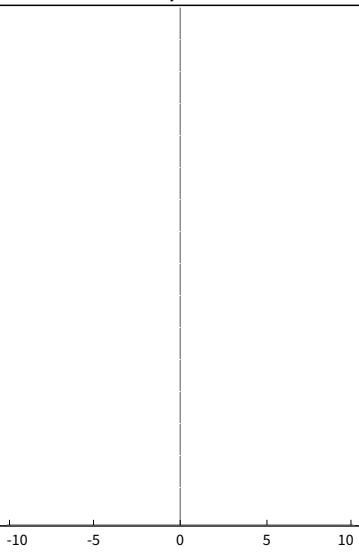


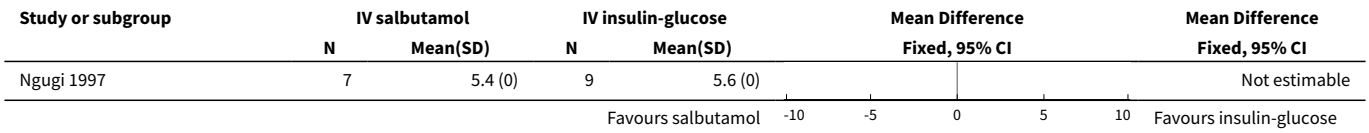
Comparison 15. IV salbutamol versus IV insulin-glucose

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 60 minutes	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 120 minutes	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.6 480 minutes	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 15.1. Comparison 15 IV salbutamol versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	IV salbutamol N	IV salbutamol Mean(SD)	IV insulin-glucose N	IV insulin-glucose Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
15.1.1 0 minutes						
Ngugi 1997	10	5.8 (0)	10	6 (0)		Not estimable
15.1.2 30 minutes						
Ngugi 1997	10	5 (0)	10	5.1 (0)		Not estimable
15.1.3 60 minutes						
Ngugi 1997	10	4.8 (0)	10	4.9 (0)		Not estimable
15.1.4 120 minutes						
Ngugi 1997	10	4.9 (0)	10	5.1 (0)		Not estimable
15.1.5 240 minutes						
Ngugi 1997	8	5.2 (0)	10	5.4 (0)		Not estimable
15.1.6 480 minutes						

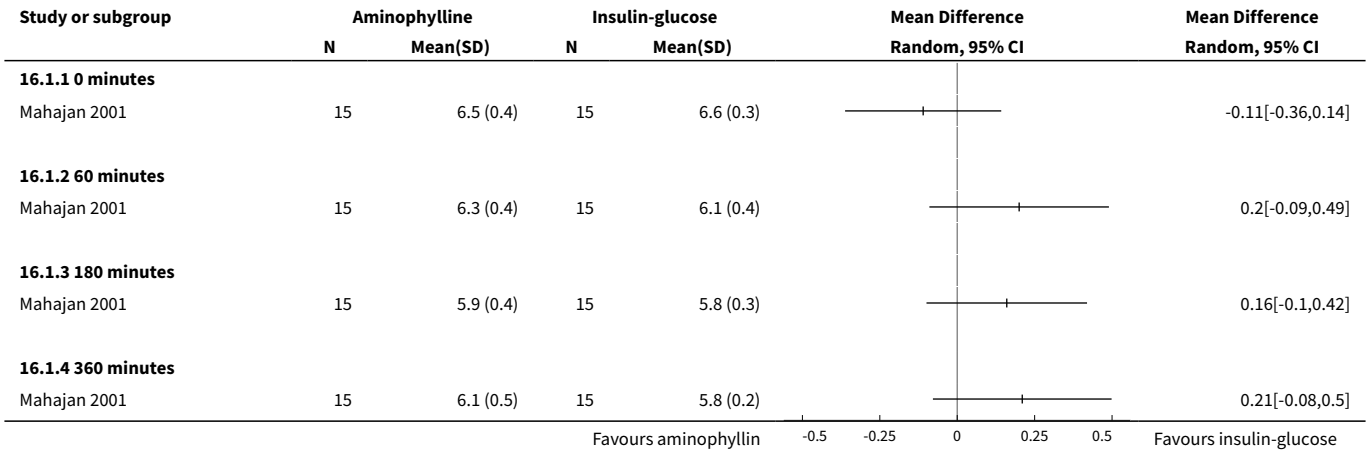




Comparison 16. IV aminophylline versus IV insulin-glucose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 360 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 16.1. Comparison 16 IV aminophylline versus IV insulin-glucose, Outcome 1 Serum potassium.



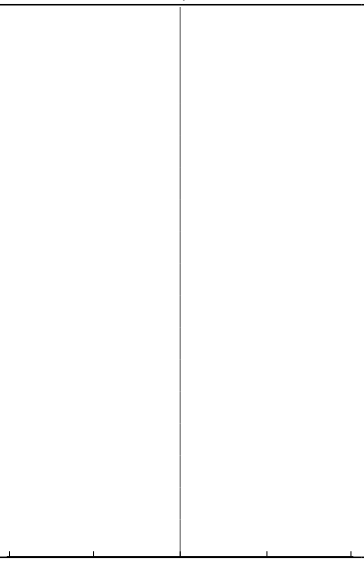
Comparison 17. IV bicarbonate versus IV insulin-glucose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.3 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 17.1. Comparison 17 IV bicarbonate versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	IV bicarbonate N	IV bicarbonate Mean(SD)	IV insulin-glucose N	IV insulin-glucose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
17.1.1 0 minutes						
Ngugi 1997	10	5.5 (0)	10	6 (0)		Not estimable
17.1.2 30 minutes						
Ngugi 1997	10	5 (0)	10	5.1 (0)		Not estimable
17.1.3 60 minutes						
Ngugi 1997	10	4.9 (0)	10	4.9 (0)		Not estimable
17.1.4 120 minutes						
Ngugi 1997	10	4.9 (0)	10	5.1 (0)		Not estimable
17.1.5 240 minutes						
Ngugi 1997	10	5 (0)	10	5.4 (0)		Not estimable
17.1.6 480 minutes						
Ngugi 1997	10	5.6 (0)	9	5.3 (0)		Not estimable

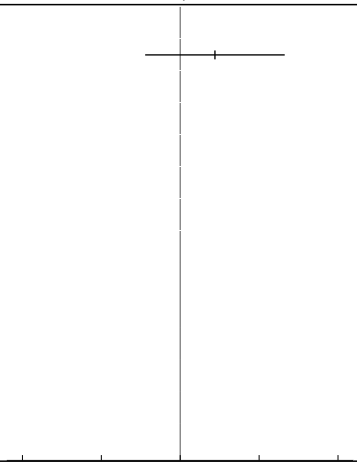


Comparison 18. IV bicarbonate plus nebulised salbutamol versus placebo

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 18.1. Comparison 18 IV bicarbonate plus nebulised salbutamol versus placebo, Outcome 1 Serum potassium.

Study or subgroup	IV bicarbonate+salbutamol N	IV bicarbonate+salbutamol Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
18.1.1 0 minutes						
Allon 1996	8	4.3 (0.5)	8	4.1 (0.3)		0.22[-0.22,0.66]
18.1.2 15 minutes						
Allon 1996	8	4.1 (0)	8	4 (0)		Not estimable
18.1.3 30 minutes						
Allon 1996	8	3.8 (0)	8	4 (0)		Not estimable
18.1.4 45 minutes						
Allon 1996	8	3.7 (0)	8	4.1 (0)		Not estimable
18.1.5 60 minutes						
Allon 1996	8	3.6 (0)	8	4.1 (0)		Not estimable

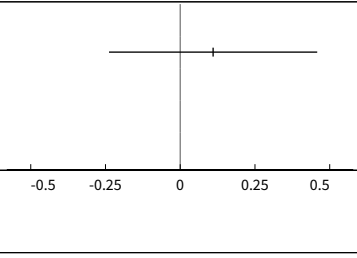


Comparison 19. IV bicarbonate plus IV insulin-glucose versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 19.1. Comparison 19 IV bicarbonate plus IV insulin-glucose versus placebo, Outcome 1 Serum potassium.

Study or subgroup	IV bicarbonate N	IV bicarbonate Mean(SD)	IV insulin-glucose N	IV insulin-glucose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
19.1.1 0 minutes						
Allon 1996	8	4.2 (0.4)	8	4.1 (0.3)		0.11[-0.24,0.46]
19.1.2 15 minutes						
Allon 1996	8	3.7 (0)	8	4 (0)		Not estimable



Study or subgroup	IV bicarbonate N	IV bicarbonate Mean(SD)	IV insulin-glucose N	IV insulin-glucose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
19.1.3 30 minutes						
Allon 1996	8	3.6 (0)	8	4 (0)		Not estimable
19.1.4 45 minutes						
Allon 1996	8	3.5 (0)	8	4.1 (0)		Not estimable
19.1.5 60 minutes						
Allon 1996	8	3.4 (0)	8	4.1 (0)		Not estimable

Favours IV bicarbonate -0.5 -0.25 0 0.25 0.5 Favours IV insulin-glucose

Comparison 20. IV insulin-glucose plus nebulised salbutamol versus IV insulin-glucose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 20.1. Comparison 20 IV insulin-glucose plus nebulised salbutamol versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	IV insulin-glucose plus nebulised salbutamol N	IV insulin-glucose plus nebulised salbutamol Mean(SD)	IV Insulin-glucose N	IV Insulin-glucose Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
20.1.1 0 minutes						
Allon 1990	12	5.9 (0.9)	12	5.5 (0.7)		0.41[-0.23,1.05]
20.1.2 15 minutes						
Allon 1990	12	5.3 (0)	12	5 (0)		Not estimable
20.1.3 30 minutes						
Allon 1990	12	5 (0)	12	4.9 (0)		Not estimable
20.1.4 45 minutes						
Allon 1990	12	4.8 (0)	12	4.8 (0)		Not estimable
20.1.5 60 minutes						
Allon 1990	12	4.8 (0)	12	4.9 (0)		Not estimable

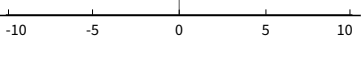
Favours IV insulin-glucose plus nebulised salbutamol -2 -1 0 1 2 Favours IV Insulin-glucose

Comparison 21. IV insulin-glucose plus IV salbutamol versus IV insulin-glucose

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 21.1. Comparison 21 IV insulin-glucose plus IV salbutamol versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	IV insulin-glucose plus IV salbutamol		IV insulin-glucose		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
21.1.1 0 minutes						
Ngugi 1997	10	6.2 (0)	10	6 (0)		Not estimable
21.1.2 30 minutes						
Ngugi 1997	10	5.2 (0)	10	5.1 (0)		Not estimable
21.1.3 60 minutes						
Ngugi 1997	10	4.8 (0)	10	4.9 (0)		Not estimable
21.1.4 120 minutes						
Ngugi 1997	10	5 (0)	10	5.1 (0)		Not estimable
21.1.5 240 minutes						
Ngugi 1997	10	5.3 (0)	10	5.4 (0)		Not estimable
21.1.6 480 minutes						
Ngugi 1997	9	5.6 (0)	9	5.6 (0)		Not estimable

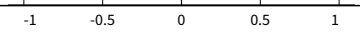


Comparison 22. IV insulin-glucose plus IV bicarbonate versus IV insulin-glucose

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 0 minutes	2	36	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.52, 0.42]
1.2 15 minutes	1	16	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 30 minutes	2	36	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1	16	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	2	36	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 120 minutes	1	20	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.7 240 minutes	1	20	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.8 480 minutes	1	19	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 22.1. Comparison 22 IV insulin-glucose plus IV bicarbonate versus IV insulin-glucose, Outcome 1 Serum potassium.

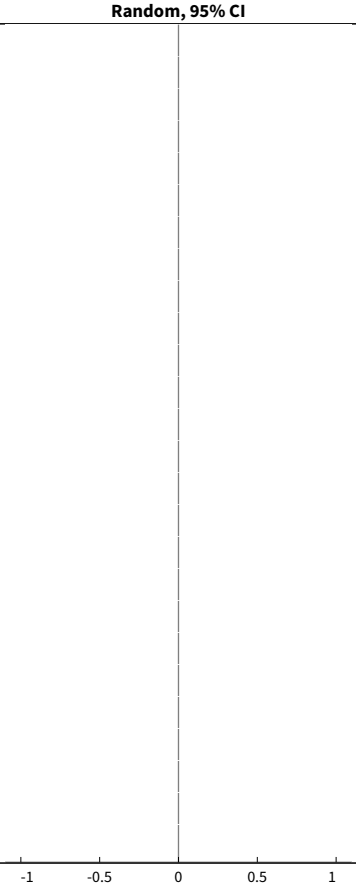
Study or subgroup	IV insulin-glucose + IV bicarbonate		IV insulin-glucose		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
22.1.1 0 minutes							
Allon 1996	8	4.2 (0.4)	8	4.3 (0.6)		100%	-0.05[-0.52,0.42]
Ngugi 1997	10	5.8 (0)	10	6 (0)			Not estimable
Subtotal ***	**18**		**18**			**100%**	**-0.05[-0.52,0.42]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.21(P=0.84)							
22.1.2 15 minutes							
Allon 1996	8	3.7 (0)	8	3.8 (0)			Not estimable
Subtotal ***	**8**		**8**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
22.1.3 30 minutes							
Allon 1996	8	3.6 (0)	8	3.6 (0)			Not estimable
Ngugi 1997	10	5 (0)	10	5.1 (0)			Not estimable
Subtotal ***	**18**		**18**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
22.1.4 45 minutes							
Allon 1996	8	3.5 (0)	8	3.5 (0)			Not estimable
Subtotal ***	**8**		**8**				**Not estimable**
Heterogeneity: Not applicable							



Favours IV insulin-glucose + IV bicarbonate

Favours V insulin-glucose

Study or subgroup	IV insulin-glucose + IV bicarbonate		IV insulin-glucose		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Test for overall effect: Not applicable							
22.1.5 60 minutes							
Allon 1996	8	3.4 (0)	8	3.4 (0)			Not estimable
Ngugi 1997	10	4.6 (0)	10	4.9 (0)			Not estimable
Subtotal ***	**18**		**18**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
22.1.6 120 minutes							
Ngugi 1997	10	4.5 (0)	10	5.1 (0)			Not estimable
Subtotal ***	**10**		**10**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
22.1.7 240 minutes							
Ngugi 1997	10	4.8 (0)	10	5.4 (0)			Not estimable
Subtotal ***	**10**		**10**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
22.1.8 480 minutes							
Ngugi 1997	10	5.1 (0)	9	5.6 (0)			Not estimable
Subtotal ***	**10**		**9**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							

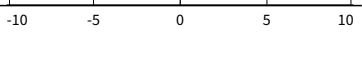


Comparison 23. IV bicarbonate plus IV salbutamol versus IV insulin-glucose

Outcome or sub-group title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 23.1. Comparison 23 IV bicarbonate plus IV salbutamol versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	IV bicarbonate + IV salbutamol		IV insulin-glucose		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
23.1.1 0 minutes						
Ngugi 1997	10	5.9 (0)	10	6 (0)		Not estimable
23.1.2 30 minutes						
Ngugi 1997	10	5.2 (0)	10	5.1 (0)		Not estimable
23.1.3 60 minutes						
Ngugi 1997	10	5 (0)	10	4.9 (0)		Not estimable
23.1.4 120 minutes						
Ngugi 1997	10	5.1 (0)	10	5.1 (0)		Not estimable
23.1.5 240 minutes						
Ngugi 1997	10	5.3 (0)	10	5.4 (0)		Not estimable
23.1.6 480 minutes						
Ngugi 1997	9	5.6 (0)	9	5.6 (0)		Not estimable

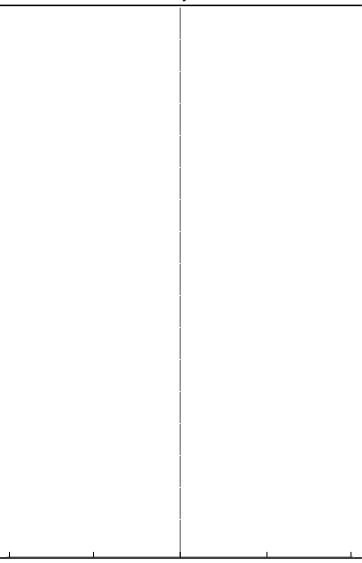


Comparison 24. IV insulin-glucose plus IV bicarbonate plus IV salbutamol versus IV insulin-glucose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 480 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 24.1. Comparison 24 IV insulin-glucose plus IV bicarbonate plus IV salbutamol versus IV insulin-glucose, Outcome 1 Serum potassium.

Study or subgroup	IV insulin-glucose + IV bicarbonate + IV salbutamol		IV insulin-glucose		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
24.1.1 0 minutes						
Ngugi 1997	10	6.6 (0)	10	6 (0)		Not estimable
24.1.2 30 minutes						
Ngugi 1997	10	5.4 (0)	10	5.1 (0)		Not estimable
24.1.3 60 minutes						
Ngugi 1997	10	5 (0)	10	4.9 (0)		Not estimable
24.1.4 120 minutes						
Ngugi 1997	10	4.9 (0)	10	5.1 (0)		Not estimable
24.1.5 240 minutes						
Ngugi 1997	10	5.3 (0)	10	5.4 (0)		Not estimable
24.1.6 480 minutes						
Ngugi 1997	9	5.6 (0)	9	5.6 (0)		Not estimable

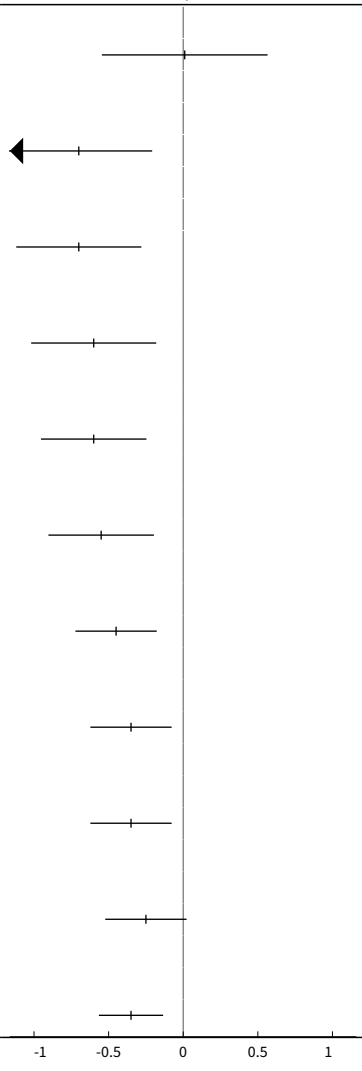


Comparison 25. Haemodialysis plus nebulised salbutamol versus haemodialysis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 50 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 70 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 90 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.6 120 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.7 150 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.8 180 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.9 210 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.10 240 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.11 270 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 25.1. Comparison 25 Haemodialysis plus nebulised salbutamol versus haemodialysis, Outcome 1 Serum potassium.

Study or subgroup	Haemodialysis + nebulised salbutamol N	Haemodialysis + nebulised salbutamol Mean(SD)	Haemodialysis N	Haemodialysis Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
25.1.1 0 minutes						
Allon 1995	7	4.5 (0.5)	7	4.5 (0.5)		0.01[-0.55,0.57]
25.1.2 30 minutes						
Allon 1995	7	3.7 (0.4)	7	4.4 (0.5)		-0.7[-1.19,-0.21]
25.1.3 50 minutes						
Allon 1995	7	3.4 (0.4)	7	4.1 (0.4)		-0.7[-1.12,-0.28]
25.1.4 70 minutes						
Allon 1995	7	3.2 (0.4)	7	3.8 (0.4)		-0.6[-1.02,-0.18]
25.1.5 90 minutes						
Allon 1995	7	3 (0.3)	7	3.6 (0.4)		-0.6[-0.95,-0.25]
25.1.6 120 minutes						
Allon 1995	7	2.9 (0.3)	7	3.5 (0.4)		-0.55[-0.9,-0.2]
25.1.7 150 minutes						
Allon 1995	7	2.9 (0.3)	7	3.3 (0.3)		-0.45[-0.72,-0.18]
25.1.8 180 minutes						
Allon 1995	7	2.9 (0.3)	7	3.2 (0.3)		-0.35[-0.62,-0.08]
25.1.9 210 minutes						
Allon 1995	7	2.9 (0.3)	7	3.2 (0.3)		-0.35[-0.62,-0.08]
25.1.10 240 minutes						
Allon 1995	7	2.9 (0.3)	7	3.1 (0.3)		-0.25[-0.52,0.02]
25.1.11 270 minutes						
Allon 1995	7	2.9 (0.3)	7	3.2 (0.1)		-0.35[-0.57,-0.13]



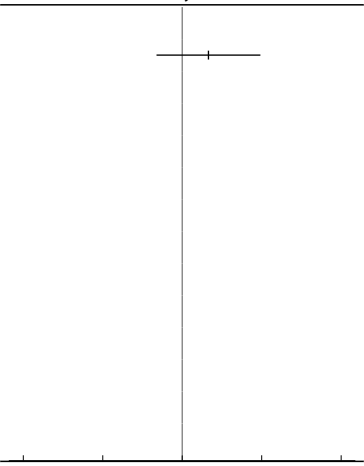
Comparison 26. IV insulin-glucose plus nebulised salbutamol versus nebulised salbutamol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Serum potassium	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1 0 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 15 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 30 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.4 45 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.5 60 minutes	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 26.1. Comparison 26 IV insulin-glucose plus nebulised salbutamol versus nebulised salbutamol, Outcome 1 Serum potassium.

Study or subgroup	IV insulin-glucose + nebulised salbutamol		Nebulised salbutamol		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
26.1.1 0 minutes						
Allon 1990	12	5.9 (0.9)	12	5.6 (0.8)		0.33[-0.32,0.98]
26.1.2 15 minutes						
Allon 1990	12	5.3 (0)	12	5.5 (0)		Not estimable
26.1.3 30 minutes						
Allon 1990	12	5 (0)	12	5.1 (0)		Not estimable
26.1.4 45 minutes						
Allon 1990	12	4.8 (0)	12	5 (0)		Not estimable
26.1.5 60 minutes						
Allon 1990	12	4.8 (0)	12	4.9 (0)		Not estimable



ADDITIONAL TABLES

Table 1. Narrative summary of results for efficacy and harm

Study	Intervention	Efficacy	Adverse Effects
Gruy-Kapral 1998	Resin-cathartics	The serum potassium concentrations before the various treatments ranged from 3.4 to 5.7 mEq/L. None of the resin-cathartic regiments caused a fall in average serum potassium concentrations, compared with prepreatment values.	None reported
Gutzwiller 2003	Haemodialysis with blood flow of 200, 250, 300 mL/min	Potassium removal was 53.0 ± 2.4, 63.4 ± 2.6, and 74.2 ± 3.8 mMol with blood flows of 200, 250, and 300 mL/min, respectively. Kt/V increased from 1.10 ± 0.14 to 1.22 ± 0.14 (10.9%) and finally to 1.39 ± 0.16 (26.4%), P = 0.0001, with increasing blood flow.	None reported
Mahajan 2001	Aminophylline infusion versus insulin-dextrose infu-	IV aminophylline lowered plasma potassium from 6.48 ± 0.39 mEq/L to 5.92 ± 0.40 mEq/L at 180 min (P < 0.001 versus basal) and 6.05 ± 0.53 mEq/L at 360 min (P <	There was one episode of hypoglycaemia in the insulin-glucose group. No

Table 1. Narrative summary of results for efficacy and harm *(Continued)*

	sion aminophyllin infusion versus insulin-dextrose infusion	0.01 versus basal). IV insulin-dextrose lowered plasma potassium from 6.59 ± 0.31 mEq/L to 5.76 ± 0.32 mEq/L (P < 0.001 versus basal) and 5.84 ± 0.21 mEq/L (P < 0.001 versus basal). Aminophylline is effective for acute treatment of hyperkalaemia but it is less effective than insulin-dextrose infusion.	other side effects were observed.
Mandelberg 1999	1200 µg salbutamol through MDS-1	Potassium levels rose from 5.5 mEq/L to 5.55 mEq/L after 1 min following completion of treatment and then decreased steadily. Potassium level decreased to 5.1 mEq/L by 60 min. The consistent reduction serium potassium levels started 3-5 min following delivery of salbutamol.	The heart rate increased from 83 ± 2 at baseline to 89 ± 2 at 1 min was greatest at 95 ± 2 at 15 min after salbutamol inhalation. The heart rate declined slightly after 1 h.
McClure 1994	Salbutamol given IV versus salbutamol nebuliser	Within 30 min of the first dose, the mean plasma potassium concentration fell significantly by 0.87 and 0.61 mmol/L after IV and nebulised administration respectively. Sixty minutes after the second dose the plasma potassium was significantly reduced by a further 0.28 and 0.53 mmol/L respectively. At the end point of the study (300 min) the level of reduction in plasma potassium in the nebulised group was significantly greater than in the group receiving salbutamol IV (1.19 compared with 0.7 mmol/L).	No major side effects were observed. Of the 10 patients who received IV salbutamol 6 had mild short lasting tremor, and 1 had mild vasomotor flushing. Of the 10 patients who received nebulized salbutamol, 4 had tremor, 2 had tremor with nausea, and one had mild vasomotor flushing.
Ngugi 1997	Dextrose and insulin, versus bicarbonate, versus salbutamol versus 2 regimen combination treatments	Of the single therapeutic approaches, at 2 h, the decrease in serum potassium caused by insulin with glucose was 0.90 ± 0.45 mmol/L (P < 0.001) which was comparable to that caused by salbutamol 0.90 ± 0.56 mmol/L (P < 0.001). Amongst the 2 regimen combinations, at 2 hours the decrease caused by salbutamol and insulin with glucose of 1.18 ± 0.69 mmol/L (P < 0.001) was comparable to that of insulin with glucose and bicarbonate of 1.19 ± 0.50 mmol/L (P = 0.002).	None reported
Pancu 2003	Nebulised albuterol versus nebulised levalbuterol	Immediately after nebulisation, only levalbuterol showed a significant decrease in potassium level (P = 0.024). Serum potassium was lowered from a baseline value of 3.9 ± 0.3 mEq/L to 3.6 ± 0.5 at 30 min post-treatment and to 3.6 ± 0.4mEq/L at 60 min post-treatment with albuterol, and from 4.1 ± 0.3 mEq/L to 3.8 ± 0.2 at 30 min and to 3.6 ± 0.2 mEq/L at 60 min with levalbuterol. No significant difference was found when the albuterol and levalbuterol groups were compared. Levalbuterol caused fewer adverse effects.	Seven patients in the albuterol group had side effects (7 had tremor, 5 nervousness, 5 palpitations, 4 had tachycardia). The 4 patients with tachycarida had heart rates between 105 and 125 beats/min. Two patients in the levalbuterol group reported tremor. One patient in the normal saline group reported nervousness and palpitations.
Zehnder 2001	Dialysate containing 0, 1, and 2 mmol/L of potassium	Serum potassium at completion of dialysis was lower with 0K compared with 1K and 2K, achieving 2.7 ± 0.1, 3.0 ± 0.2 and 3.5 ± 0.1mmol/L (P < 0.001) respectively. The amount of potassium removed was significantly different between the 3 regimens used. Potassium removal was 117.1 ± 10.3 mmol for 0K, 80.2 ± 6.2 mmol for 1K, and 63.3 ± 5.2 mmol for 2K (P < 0.001). Potassi-	None reported.

Table 1. Narrative summary of results for efficacy and harm *(Continued)*

		um free dialysate removed 85% more potassium than 2K and 46% more than 1K.	
Allon 1990	IV insulin with glucose, nebulised albuterol or combination of IV insulin with glucose and nebulised albuterol	IV insulin with glucose produced a fall in plasma potassium apparent within 15 min of drug administration and persisted for at least one hour. Nebulised albuterol resulted in a decrease in plasma K within 30 min of initiating treatment. The mean decrease in plasma potassium was not different at 30, 45, or 60 min following the 2 respective treatments. The maximal decrease was 0.65 ± 0.09 and 0.66 ± 0.12 mmol/L after insulin with glucose and albuterol, respectively. The magnitude of fall in plasma potassium was greater with combined IV insulin and glucose and nebulized albuterol. the maximal decrease in mean plasma potassium concentration after insulin with glucose plus albuterol was 1.21 ± 0.19 mmol/L.	There were no statistically significant changes in blood pressure or heart rate following any of the treatments. Combined drug therapy (IV insulin with glucose and nebulised salbutamol) was associated with a increase in heart rate of 15.1 ± 6.0 beats/min at 60 min (P < 0.02).
Allon 1996	Isotonic bicarbonate, insulin and albuterol, and the above in combination with bicarbonate	IV bicarbonate did not decrease plasma potassium during 60 min of observation. IV insulin with dextrose decreased plasma potassium 0.5 mmol/L (P < 0.001) within 15 min and progressed for the duration of infusion. The magnitude of change at 60 min did not differ whether insulin was given with isotonic bicarbonate or saline (-0.81 ± 0.15 mmol/L versus -0.85 ± 0.06 mmol/L; P = 0.65). Nebulised albuterol decreased plasma potassium by 0.2 mmol/L at 15 min and progressed for the duration of the infusion. The magnitude of change at 60 min did not differ whether albuterol was given with isotonic bicarbonate or saline (0.71 ± 0.16 mmol/L versus -0.53 ± 0.15 mmol/L; P = 0.18).	The 3 protocols that included bicarbonate administration resulted in significant increases in blood bicarbonate (+3.5 ± 0.5 mmol/L, +3.1 ± 0.5 mmol/L, and +2.2 ± 0.5 mmol/L, P < 0.005) and pH (+0.05 ± 0.01, +0.03 ± 0.01, and +0.03 ± 0.01, P < 0.01). Administration of insulin with glucose increased plasma glucose to high physiologic concentrations (P < 0.05) at all time points between 15 and 60 min. Nebulised albuterol produced a mild increase in plamsa glucose (P < 0.05) at time points between 30 and 60 min.
Allon 1989	Nebulised albuterol (10 mg or 20 mg) or placebo	Nebulised albuterol therapy resulted in a significant fall in the plasma potassium concentration within 30 min of drug administration that persisted for at least 2 hours. The maximal mean decrease in the potassium concentration was 0.62 ± 0.09 mmol/L after the 10 mg dose and 0.98 ± 0.14 mmol/L after the 20 mg dose (P < 0.001 for both comparisons). At all periods between 30 and 120 min, the decrease in the plasma potassium concentraion was significantly greater than that measured in the corresponding period of placebo administration. The potassium-lowering effect of the 20 mg dose was greater than that of the 10 mg dose, but this difference achieved statistical significance only at 120 min.	No significant changes in blood pressure or heart rate with albuterol treatment. All patients denied palpitations, tremor, or chest pain after inhalation of albuterol. One patient had mild anxiety after a 20 mg dose of albuterol.
Allon 1995	Nebulised albuterol (20 mg) or placebo in addition to hemodialysis treatment	Plasma potassium decreased significantly 30 min after nebulised albuterol therapy compared to placebo in the pre-dialysis period. Dialysis decreased plasma potassium in both groups, but plasma potassium in the albuterol treatment group has persistently lowered lev-	Albuterol produced a significant increase in heart rate 30 minutes after its administration (79 ± 4 pretreatment, 103 ± 5 predialysis/30

Table 1. Narrative summary of results for efficacy and harm *(Continued)*

	el than placebo. However, the total potassium removal is significantly less in the albuterol group.	min after administration, P < 0.001). Rare unifocal premature ventricular contractions were noted in 5/7 patients in the albuterol protocol and in 2/7 patients in the control protocol during the last 2 hours of dialysis. One patient with a history of paroxysmal atrial fibrillation developed asymptomatic atrial fibrillation after albuterol administration that resolved spontaneously.

WHAT'S NEW

Date	Event	Description
15 September 2016	Review declared as stable	This review has been replaced by "Pharmacological interventions for the acute management of hyperkalaemia in adults". 10.1002/14651858.CD010344.pub2

HISTORY

Protocol first published: Issue 3, 2001
Review first published: Issue 2, 2005

Date	Event	Description
13 May 2009	Amended	Contact details updated.
29 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

- Mahoney & Smith conducted the first phase of the review, up to 2000.
- Lo and Tsoi conducted the second phase of the review, 2000-2004.
- Tonelli researched the non-randomized literature for calcium studies to include in the discussion.
- Clase supervised the project.
- All reviewers were involved in writing and reviewed the full manuscript.

DECLARATIONS OF INTEREST

None known

NOTES

September 2016: this review has been replaced by "Pharmacological interventions for the acute management of hyperkalaemia in adults". 10.1002/14651858.CD010344.pub2

INDEX TERMS

Medical Subject Headings (MeSH)

*Emergency Treatment; Adrenergic beta-Agonists [therapeutic use]; Albuterol [therapeutic use]; Bicarbonates [therapeutic use]; Glucose [therapeutic use]; Hyperkalemia [*therapy]; Hypoglycemic Agents [therapeutic use]; Infusions, Intravenous; Insulin [therapeutic use]; Randomized Controlled Trials as Topic; Renal Dialysis

MeSH check words

Humans