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| Question | |
| **Should insulin with glucose or salbutamol vs. no insulin with glucose and no salbutamol be used for paediatric patients in CA suspected to be caused by hyperkalaemia?** | |
| **Population:** | paediatric patients in CA suspected to be caused by hyperkalaemia |
| **Intervention:** | insulin with glucose or salbutamol |
| **Comparison:** | no insulin with glucose and no salbutamol |
| **Main outcomes:** | Survival to discharge; Survival to discharge with favourable outcome (PCPC1-3 or no change from baseline); Survival to discharge with PCPC 1 or 2 or no change from baseline; |
| **Setting:** | Any setting |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** | none |

# Assessment

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| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know | Paediatric cardiac arrest is rare and patients with hyperkalaemia are only a minority of these patients. So it is not a problem on population level. However, the optimal management strategy is indeed a priority for the individual patients who might arrest due to acute hyperkalaemia such as patients with renal failure, tumor lysis syndrome, massive tissue damage (crush syndrome), malignant hypertermia etc. |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | The salbutamol was proven to have potassium lowering effect in the performed meta-analysis of the patients not in cardiac arrest(1, 2, 3, 4, 5, 6, 7, 8). It was not possible to perform meta-analysis of the studies with insulin with glucose because of the heterogeneity(9, 10, 11). However, the potassium lowering effect was proven in meta-analysis in adult patients for different doses.  The magnitude of the potassium lowering effect in the cardiac arrest patient population is unclear. | The potassium lowering effect of the insulin with glucose as well as of the salbutamol IV requires up to 30-60 minutes in patients not in cardiac arrest. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know | Since the population of patients in cardiac arrest due to hyperkalemia is small, the undersirable effects are trivial. There might be theoretical cumulative effect of salbutamol with adrenaline on the beta-receptors and insulin which could cause hypoglycemia. |  |
| Certainty of evidence What is the overall certainty of the evidence of effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ○ Low ○ Moderate ○ High ● No included studies | No pediatric studies were identified. |  |
| Values Is there important uncertainty about or variability in how much people value the main outcomes? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability | The p-COSCA outcomes were assessed as the most important outcomes. It is not clear whether the parents of the children after cardiac arrest value those specific outcomes equally as the researchers and clinicians. However, for the p-COSCA critical outcomes (survival with favourable neurological outcome and survival with PCPCP 1-2 or no change from baseline) there probably is not be uncertainty that these are desired outcomes for parents as well as for clinicians, as well as desired outcomes on the population level. |  |
| Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ● Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know | The potassium lowering effect was proven in the population of pediatric patients not in cardiac arrest in the systematic review performed for salbutamol. For insulin with glucose, the meta-analysis could not be performed but the potassium lowering effect was consistent in adult population. The safety profile of these interventions was good. Adverse events included mainly tachycardia for salbutamol and hypo- or hyperglycemia for insulin with glucose. All were usually mild and non life-threatening. |  |
| Resources required | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know | Insulin with glucose and salbutamol are both inexpensive medications. However, there might be places where they are not easily available to everyone and the implementation of the good practice statement might add additional costs. |  |
| Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ○ Low ○ Moderate ○ High ● No included studies |  |  |
| Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies |  |  |
| Equity What would be the impact on health equity? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know |  | There might be places where the insulin with glucose or salbutamol IV might not be easily available to everyone and the implementation might add additional costs. |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know |  | Although the intervention is likely well accepted in high-resource settings, it can be more difficult in the limited-resource setting (costs, personnel). |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know |  | Same as above. |

# Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Certainty of evidence** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | **Varies** | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | Probably yes | Yes |  | Varies | **Don't know** |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

# Type of recommendation

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| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# Conclusions

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| Recommendation |
| We suggest using intravenous salbutamol or insulin with glucose or combination of both to lower the potassium levels in paediatric patients with cardiac arrest associated with hyperkalaemia with the aim to lower the potassium levels during the concurrently ongoing high-quality resuscitation efforts (Good Practice Statement). |
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| Justification |
| The effects on potassium levels in the cardiac arrest patients were not studied so it is not clear whether the potassium-lowering effect would be present also in cardiac arrest patients. However, the Task Force agreed that the potential benefits of these pharmacological interventions outweigh potential risks in the cardiac arrest patients and their use is therefore justified.  Despite limited evidence for clinical outcomes, an initial treatment strategy aiming at acutely lowering extracellular potassium levels simultaneously with more permanent potassium lowering strategies seems logical when hyperkalaemia is a suspected reversible cause of cardiac arrest. Only beta2-agonists were proven to have potassium lowering effect in paediatric patients by meta-analysis in the systematic review. Inhalation administration is generally not recommended in cardiac arrest. Insulin with glucose for the potassium lowering effect was studied in the pediatric patients but the high heterogeneity of the studies precluded the meta-analysis. PLS TF agreed that they would use insulin with glucose in case of suspected hyperkalemia despite the lack of high quality studies in pediatric patients. The insulin with glucose was used in this indication and it has proven potassium lowering effect in adult population. |

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| Subgroup considerations |
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| Implementation considerations |
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| Monitoring and evaluation |
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| Research priorities |
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