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| Question | |
| **Should calcium vs. no calcium be used for paediatric CA caused by hyperkalaemia?** | |
| **Population:** | paediatric CA caused by hyperkalaemia |
| **Intervention:** | calcium |
| **Comparison:** | no calcium |
| **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 use of calcium was not associated with harm in the subgroup of patients with hyperkalaemia but the desired outcomes were not significantly different for the use of calcium vs. no calcium. (1) | The use of calcium was generally associated with worse outcomes in the overall cohort of paediatric patients with cardiac arrest. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | Calcium use was associated with worse outcomes in the overall population of paediatric patients with cardiac arrest. The effect of calcium in patients with hyperkalaemia is is unclear (e.g. in patients with cardiac arrest and lactacidemia) but possibly can be associated with worse outcomes. (1) | Calcium use in OHCA adult patients with hyperkalaemia was associated with worse outcomes (Wang, 2016) |
| 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 | The data were only from one registry-based study and the certainty of evidence was considered very low. | One animal study showed no benefit of calcium in cardiac arrest caused by hyperkalaemia. One adult study showed calcium use was associated with worse outcomes in OHCA with hyperkalaemia (2). |
| 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 baselineit is likely that there is minimal uncertainty that these are desired outcomes for parents as well as for clinicians and also 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 |  |  |
| Resources required | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know | The cost of calcium if used is relatively low. The other resources will not differ between the groups with or without the calcium. |  |
| 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 |  | Calcium is inexpensive. But one need to consider the negative effects on cardiac arrest in general which are negative. |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Calcium is commonly used during pediatric cardiac arrest although its effect is questionable and generally is associated with worse outcomes. (1) |  |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know |  |  |

# Summary of judgements

|  | **Judgement** | | | | | | |
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| **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 |
| For the pediatric patients in cardiac arrest suspected to be caused by hyperkalaemia, there is insufficient evidence to suggest for or against the use of calcium. |
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| Justification |
| The very low certainty evidence suggests association of calcium with worse outcomes but there are critical risks of bias and high uncertainty of associated effects mainly due to resuscitation time (duration of resuscitative efforts) bias. However, even in patients without cardiac arrest, any evidence of calcium having effect on ECG pathology was not shown in the systematic review performed. Therefore, the rationale behind the use of calcium for the assumed myocardium protecting effect is being questioned. |

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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 |
| The role of calcium as a protection of myocardial cells from hyperkalaemia is recently questioned and the published studies do not support its presumed usefulness. More studies are needed to better understand this topic. |

# References Summary

1. Cashen, K., Sutton, R. M., Reeder, R. W., Ahmed, T., Bell, M. J., Berg, R. A., Burns, C., Carcillo, J. A., Carpenter, T. C., Michael Dean, J., Wesley Diddle, J., Federman, M., Fink, E. L., Franzon, D., Frazier, A. H., Friess, S. H., Graham, K., Hall, M., Hehir, D. A., Horvat, C. M., Huard, L. L., Kirkpatrick, N. T., Maa, T., Manga, A., McQuillen, P. S., Morgan, R. W., Mourani, P. M., Nadkarni, V. M., Naim, M. Y., Notterman, D., Page, K., Pollack, M. M., Qunibi, D., Sapru, A., Schneiter, C., Sharron, M. P., Srivastava, N., Viteri, S., Wessel, D., Wolfe, H. A., Yates, A. R., Zuppa, A. F., Meert, K. L.. Calcium use during paediatric in-hospital cardiac arrest is associated with worse outcomes.Resuscitation; Apr 2023.

2. Wang, C. H., Huang, C. H., Chang, W. T., Tsai, M. S., Yu, P. H., Wu, Y. W., Hung, K. Y., Chen, W. J.. The effects of calcium and sodium bicarbonate on severe hyperkalaemia during cardiopulmonary resuscitation: A retrospective cohort study of adult in-hospital cardiac arrest.Resuscitation; Jan 2016.