Question

Should MAGNESIUM vs No Magnesium be used for adults with shock refractory VF/pVT

PROBLEM:	Shock refractory VF/pVT	**BACKGROUND:**	Mg is not recommended for routine use as an alternative anti-arrhythmic in refractory VF/pVT),
OPTION:	MAGNESIUM plus standard care		
COMPARISON:	Placebo plus standard care		
MAIN OUTCOMES:	Survival to discharge with good neuro/ survival to discharge/ROSC		
SETTING:	OHCA/IHCA		
PERSPECTIVE:	Patient perspective		

Assessment

<table>
<tr><th></th><th>JUDGEMENT</th><th>RESEARCH EVIDENCE</th><th>ADDITIONAL CONSIDERATIONS</th></tr>
<tr><td>PROBLEM</td><td>Is the problem a priority?

○ No
○ Probably no
○ Probably yes
○ <u>Yes</u>

○ Varies
○ Don't know</td><td>Only those cases where VF/pVT persists after defibrillation attempts require an antiarrhythmic drug. In a large RCT (n= 23,711) of continuous or interrupted chest compressions during cardiopulmonary resuscitation (CPR) for OHCA (Nichol 2015 2203), 22.5% of patients had an initial rhythm of VF/pVT and about 6.7% of all patients received an antiarrhythmic drug (amiodarone 4.7%, lidocaine 2.0%) during CPR.
<table><tr><td>Lidocaine — no./total no. (%)</td><td>246/12,629 (1.9)</td><td>229/11,034 (2.1)</td><td>0.46</td></tr><tr><td>Amiodarone — no./total no. (%)</td><td>561/12,629 (4.4)</td><td>541/11,034 (4.9)</td><td>0.37</td></tr></table>A large observational study (n= 108,079) on airway management using data from the American Heart Association Get With The Guidelines Registry of IHCA reported that about 18% of all patients had an initial rhythm of VF/pVT, and 25% of all patients received an antiarrhythmic drug (amiodarone 17%, lidocaine 8%) during CPR (Andersen 2017 494).

This update about the role of antiarrhythmic drugs was prioritized by the ALS Task Force following publication of a large RCT comparing amiodarone, lidocaine and placebo (‘ROC ALPS’) (Kudenchuk 2016 1711) which was published after the CoSTR in 2015 (Callaway 2015 s84, Soar 2015 e71).</td><td>NO NEW EVIDENCE FOR MAGNESIUM IDENTIFIED SINCE 2015 ILCOR COSTR</td></tr>
<tr><td>DESIRABLE EFFECTS</td><td>How substantial are the desirable anticipated effects?

○ Trivial
○ Small
○ Moderate
○ Large

○ Varies
○ <u>Don't know</u></td><td><table><tr><th>Outcomes [importance]</th><th>№ of participants (studies)</th><th>Certainty of the evidence (GRADE)</th><th>Relative effect (95% CI)</th><th colspan="2">Anticipated absolute effects</th></tr><tr><th></th><th></th><th></th><th></th><th>Risk with standard care</th><th>Risk difference with Intervention + standard care</th></tr><tr><td colspan="6">Magnesium versus placebo</td></tr><tr><td>Survival to hospital discharge with good neurological outcome [Critical]</td><td>332 (3 RCTs)</td><td>Very Low</td><td>RR 2.08 (0.87 to 4.97)</td><td>35 per 1,000</td><td>38 more per 1,000 (from 5 fewer to 140 more)</td></tr><tr><td>Survival to hospital discharge [Critical]</td><td>437 (4 RCTs)</td><td>Very Low</td><td>RR 1.07 (0.62 to 1.86)</td><td>90 per 1,000</td><td>6 more per 1,000 (from 34 fewer to 77 more)</td></tr><tr><td>Return of spontaneous circulation [Important]</td><td>437 (4 RCTs)</td><td>Very Low</td><td>RR 0.97 (0.77 to 1.24)</td><td>327 per 1,000</td><td>4 more per 1,000 (from 83 less to 92 more)</td></tr></table></td><td>All studies small, published pre 2001, The four available RCTs had a total of 437 patients, and the most recent was published in 2002 and followed the 1992 ERC guidelines (Fatovich 1997 237, Thel 1997 1272, Allegra 2001 245, Hassan 2002 57). In addition, in two of these study not all included patients had an arrest rhythm of VF/pVT (Fatovich 1997 237, Thel 1997 1272).</td></tr>
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UNDESIRABLE EFFECTS	**How substantial are the undesirable anticipated effects?** ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ○ **Don't know**		
CERTAINTY OF EVIDENCE	**What is the overall certainty of the evidence of effects?** ○ **Very low** ○ Low ○ Moderate ○ High ○ No included studies	**Very low certainty**	
VALUES	**Is there important uncertainty about or variability in how much people value the main outcomes?** ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ **No important uncertainty or variability**		Most people would agree on survival to hospital discharge, Survival with good neurology at hospital discharge. Longer term outcomes, HRQoL not addressed in available studies
BALANCE OF EFFECTS	**Does the balance between desirable and undesirable effects favor the intervention or the comparison?** ○ 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	No	

RESOURCES REQUIRED	**How large are the resource requirements (costs)?** ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ **Don't know**	No formal cost-effectiveness studies performed.	Will vary across ILCOR Councils.
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**What is the certainty of the evidence of resource requirements (costs)?** ○ Very low ○ Low ○ Moderate ○ High ○ **No included studies**	No studies identified.	
COST EFFECTIVENESS	**Does the cost-effectiveness of the intervention favor the intervention or the comparison?** ○ 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**	No studies identified.	Not formally studied
EQUITY	**What would be the impact on health equity?** ○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ **Don't know**	Uncertain, no relevant studies identified.	

ACCEPTABILITY	**Is the intervention acceptable to key stakeholders?** ○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ **Don't know**	Currently not used/recommended	Not part of routine use, although used in special circumstances in some settings
FEASIBILITY	**Is the intervention feasible to implement?** ○ No ○ Probably no ○ Probably yes ○ **Yes** ○ Varies ○ Don't know	Many services already use IV drugs	Mg available

Summary of judgements

	JUDGEMENT							IMPLICATIONS
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know	
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know	
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		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	

Conclusions - MAGNESIUM vs No Magnesium be used for adults with shock refractory VF/pVT

TYPE OF RECOMMENDATION	Strong recommendation against the option ○	**Conditional recommendation against the option** ○	Conditional recommendation for either the option or the comparison ○	Conditional recommendation for the option ○	Strong recommendation for the option ○
RECOMMENDATION	We suggest against the routine use of magnesium in adult patients with refractory VF/pVT (weak recommendation, low-quality evidence).				
JUSTIFICATION	No evidence of benefit, and not currently recommended for routine use				
SUBGROUP CONSIDERATIONS	In making a suggestion against the routine use of magnesium for refractory VF/pVT cardiac arrest, we recognize that there are specific circumstances where magnesium could be considered during refractory VF/pVT (e.g. hypomagnesemia, torsade de pointes). These were not formally reviewed.				
IMPLEMENTATION CONSIDERATIONS	Not currently routinely used				
MONITORING AND EVALUATION	Use of anti-arrhythmic drugs should be included in OHCA and IHCA registry data.				
RESEARCH PRIORITIES	We discussed if magnesium has a beneficial overall effect in cardiac arrest – e.g. neurological outcome, as opposed to antiarrhythmic effect.				