Supraglottic airway device versus tracheal intubation in the initial airway management of out-of-hospital cardiac arrest: the AIRWAYS-2 cluster RCT

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Scientific summary

The AIRWAYS-2 cluster RCT

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Scientific summary

Background

In the UK the incidence of out-of-hospital cardiac arrest is 123 cases per 100,000 population per annum. Optimal cardiopulmonary resuscitation and rapid return of spontaneous circulation are associated with avoiding or minimising neurological impairment in the survivors of out-of-hospital cardiac arrest, and early effective airway management, which involves techniques to maintain a clear and unobstructed airway, is fundamental to this.

Tracheal intubation is the placement of a plastic tube into the trachea (windpipe) to keep an open airway. Traditional teaching suggests that tracheal intubation is the most effective way to manage the airway during out-of-hospital cardiac arrest. However, pre-hospital intubation attempts by paramedics can cause complications such as interruptions in chest compressions and unrecognised tube misplacement. Supraglottic airway devices are an alternative to intubation. They are placed just above the larynx, rather than in the trachea, are quicker and easier to insert and may avoid the complications of tracheal intubation. Supraglottic airway devices are used safely to manage the airway during routine anaesthesia and are in widespread use in NHS ambulance services.

Equipoise between the two techniques led to calls for a large randomised controlled trial to compare them. Relatively small gains in survival of 2–3% would be clinically meaningful and worthwhile, provided that the intervention is cost-effective.

Objectives

Main trial

The aim of the AIRWAYS-2 trial was to determine whether or not the i-gel® (Intersurgical Ltd, Wokingham, UK), a second-generation supraglottic airway device, is superior to tracheal intubation in non-traumatic out-of-hospital cardiac arrest in adults, in terms of both clinical efectiveness and cost-effectiveness.

The trial objectives were to estimate:

- The difference in the primary outcome of modified Rankin Scale score at hospital discharge (or 30 days post out-of-hospital cardiac arrest if the patient was still in hospital) between groups of patients managed by paramedics randomised to use either i-gel or tracheal intubation as their initial advanced airway management strategy following out-of-hospital cardiac arrest. The modified Rankin Scale is a functional status outcome used to measure disability or dependence in the daily activities of people.
- Differences in secondary outcome measures relating to airway management, hospital stay and recovery at 3 and 6 months between groups of patients managed by paramedics randomised to use either i-gel or tracheal intubation.
- The relative cost-effectiveness of i-gel compared with tracheal intubation, including estimation of major in-hospital resource use, and associated costs in each group.

Economic evaluation

The economic evaluation aimed to estimate the incremental cost-effectiveness of the i-gel compared with tracheal intubation in adult non-traumatic out-of-hospital cardiac arrest in line with the AIRWAYS-2 trial.

Design

The AIRWAYS-2 trial was a pragmatic, open, parallel, two-group, multicentre, cluster randomised controlled trial. The trial objectives were addressed by randomising paramedics, rather than patients, to either i-gel or tracheal intubation. Paramedics used their allocated device at all eligible out-of-hospital cardiac arrests for the duration of the trial.

Setting

The trial involved four NHS ambulance services and the 95 NHS hospitals served by these ambulance services. The four ambulance services covered 21 million people (40% of England's population). All eligible patients attended by an AIRWAYS-2 paramedic (i.e. a paramedic who provided consent and was randomised) between June 2015 and August 2017 were automatically enrolled in the trial.

Participants

Paramedics were eligible if they were employed by one of the four participating ambulance services and could be despatched to attend an out-of-hospital cardiac arrest as the first or second paramedic to arrive at the patient's side. They had to be qualified to practise tracheal intubation in their clinical role.

The trial population was adults who had a non-traumatic out-of-hospital cardiac arrest. The trial inclusion criteria were:

- patient known or believed to be aged $\geq$ 18 years
- non-traumatic cardiac arrest outside hospital
- patient attended by a paramedic who is participating in the trial and is either the first or second paramedic to arrive at the patient's side
- resuscitation commenced or continued by ambulance staff or responder.

Interventions

The interventions studied were use of an i-gel, a second-generation supraglottic airway device, and tracheal intubation, the placement of a cuffed tube in the patient's trachea. Both provide oxygen to the lungs and remove carbon dioxide. Tracheal intubation is generally considered the 'gold standard' of airway management and is used universally in comatose survivors of cardiac arrest following their admission to hospital.

Main outcome measures

Main trial

The primary outcome was modified Rankin Scale score measured at hospital discharge (or 30 days post out-of-hospital cardiac arrest if the patient was still in hospital). The modified Rankin Scale is widely used in out-of-hospital cardiac arrest research and comprises a seven-point scale (0 to 6). This is usually dichotomised as good (0–3) or poor outcome/death (4–6; 6 indicates death).

The following secondary outcomes were collected for all eligible patients, with all but the last two reported by participating paramedics:

- initial ventilation success (visible chest rise)
- regurgitation (stomach contents visible in the mouth or nose) and aspiration (stomach contents visible below the vocal cords or inside a correctly placed tracheal tube or airway channel of a supraglottic airway device)
- loss of a previously established airway (patients with advanced airway management only)
- sequence of airway interventions delivered (patients with advanced airway management only)
- rapid return of spontaneous circulation
- airway management in place when rapid return of spontaneous circulation was achieved or resuscitation was discontinued
- chest compression fraction (in a subset of patients in two ambulance services)
- time to death.

For patients who survived to hospital admission, length of intensive care stay and length of hospital stay were also collected. For patients who survived to hospital discharge, health-related quality of life using the EuroQol-5 Dimensions, five-level version, was collected at the time of discharge. For patients who survived beyond hospital discharge, date of death was collected (if applicable), modified Rankin Scale score was collected at 3 and 6 months post out-of-hospital cardiac arrest, and quality of life was collected using the EuroQol-5 Dimensions, five-level version, at 3 and 6 months post out-of-hospital cardiac arrest.

Economic evaluation

The primary outcome measure for the cost-effectiveness analysis was quality-adjusted life-years, estimated using the EuroQol-5 Dimensions, five-level version.

Methods

Main trial

In the AIRWAYS-2 trial, potential participants were unconscious and in need of immediate emergency care, and clinical necessity was therefore the over-riding priority. For this reason, it was not considered practical to design the trial to randomise individual patients, and a cluster randomised design was adopted. We randomised paramedics, treating each participating paramedic as a 'cluster'. Paramedics who consented to participate in the trial were randomly allocated in a 1 : 1 ratio to one of the two groups: i-gel or tracheal intubation. This ensured that the number of paramedics in each group was equal. However, some imbalance in the number of patients enrolled was possible as a result of chance.

Randomisation was performed using a secure computer system, with allocation concealment. Allocation could not be changed once assigned.

Data collection included the following elements:

- a log of all paramedics approached and a record of those who consented to take part in the trial
- a log of all patients who had an out-of-hospital cardiac arrest who were attended by a paramedic in one of the four participating ambulance trusts
- a log of those attended by an AIRWAYS-2 paramedic
- a log of all out-of-hospital cardiac arrest patients attended by an AIRWAYS-2 paramedic (where resuscitation was attempted) assessed against the eligibility criteria and, if ineligible, reasons for ineligibility
- a screening log of all out-of-hospital cardiac arrest patients enrolled in the trial who survived to intensive care unit/coronary care unit discharge

- survivors who were approached for consent and outcome of the consent process
- for those who consented to active follow-up, responses to quality-of-life and modified Rankin Scale questionnaires collected at the time of consent and at follow-up at 3 and 6 months
- key data items from routine data sources for survivors who provided consent and for those who died prior to discharge from intensive care unit/coronary care unit
- demographic characteristics of surviving out-of-hospital cardiac arrest patients who did not consent and withdrew from the trial.

These data were requested without any direct patient identifiers to maintain anonymity.

Data collection occurred during the out-of-hospital treatment phase, during the inpatient phase of care, at hospital discharge and at 3 and 6 months (± 4 weeks) after the index out-of-hospital cardiac arrest.

Economic evaluation

A cost-effectiveness analysis (specifically a cost–utility analysis) using quality-adjusted life-years as the primary outcome measure was conducted, as advocated by the National Institute for Health and Care Excellence. Incremental costs (the difference in mean costs between the i-gel and tracheal intubation groups) were divided by incremental quality-adjusted life-years (the difference in mean quality-adjusted life-years between the groups) and presented as the incremental cost-effectiveness ratio, which quantifies the incremental cost per quality-adjusted life-year gained by switching from tracheal intubation to the i-gel. The economic evaluation analyses were performed on an intention-to-treat basis. The i-gel was considered cost-effective if the incremental cost-effectiveness ratio fell below £20,000, which is the willingness-to-pay threshold that the National Institute for Health and Care Excellence adopts.

Resource use data were collected on all significant health service resource inputs for trial patients to the end of the 6-month follow-up period. Detailed resource use data on the pre-hospital phase in the patient care pathway were collected on the trial case report forms, and inpatient data were obtained mostly from Hospital Episode Statistics data sets; some resource use data items were captured on in-hospital case report forms. Case report forms for the pre-hospital phase were completed by the paramedics attending the out-of-hospital cardiac arrests and by a research paramedic employed in each ambulance trust from the computerised ambulance service system. Primary and community care resource use post hospital discharge was captured using follow-up questionnaires at 3 and 6 months post out-of-hospital cardiac arrest for patients who consented to follow-up.

Results

Main trial

A total of 2041 paramedics from the four participating NHS ambulance trusts expressed an interest in participating in the trial. A total of 1523 paramedics were recruited and randomised (764 randomised to tracheal intubation and 759 randomised to i-gel). The first paramedic randomisation occurred in March 2015.

During the trial, 73,893 out-of-hospital cardiac arrests were attended and a total of 29,733 (40.2%) patients received a resuscitation attempt; 13,462 (45.3%) of these were cases in which an AIRWAYS-2 paramedic was first or second to the patient's side. A total of 4164 patients were found to be ineligible. Eligibility status was unknown for two patients. Overall, 9296 eligible patients were attended by 1382 trial paramedics. Seven patients did not have primary outcome data: four because of an inability to identify the patient and three because the patient was admitted to a non-participating hospital. Therefore, 9289 patients were included in the analysis of the primary outcome.

With regard to airway management of patients, 7580 patients received advanced airway management, of whom 2840 received tracheal intubation first, 4632 received i-gel first and 108 received a non-i-gel supraglottic airway device first.

Similar proportions of patients in the two treatment groups had a favourable functional outcome (modified Rankin Scale score) at 30 days/hospital discharge (tracheal intubation group, 6.8%; i-gel group, 6.4%). Crossover was more common among patients randomised to tracheal intubation than among those randomised to i-gel.

Economic evaluation

Mean quality-adjusted life-years to 6 months were 0.03 in both groups (i-gel minus tracheal intubation difference −0.0015, 95% confidence interval −0.0059 to 0.0028). The total costs of care from out-of-hospital cardiac arrest up to 6 months were £3570 and £3413 in the i-gel and tracheal intubation groups, respectively (mean difference £157, 95% confidence interval −£270 to £583). Based on the point estimate of cost-effectiveness only, tracheal intubation was more effective and less costly than i-gel (i.e. dominant) and, therefore, cost-effective. However, bootstrap replicates of these differences covered three quadrants of the cost-effectiveness plane, demonstrating great uncertainty around these results, indicating no evidence of an overall difference in cost-effectiveness between the groups.

Limitations

This trial had several limitations. First, there was an imbalance in the number of patients in the two groups, probably due to unequal distribution of high-enrolling paramedics in the two groups; it was not possible to stratify for this because high-enrolling paramedics could not be identified in advance. Second, there was crossover between groups, which was inevitable on practical and ethics grounds. Third, although other elements of care followed established guidelines, differences in these factors between groups could have influenced the findings. Fourth, the participating paramedics were volunteers and their airway skills may not be representative of those who chose not to take part. Fifth, the findings are applicable to use of i-gel in countries with similar emergency medical services provision to England, where paramedics attend most out-of-hospital cardiac arrests. The findings may not be applicable in countries with physician-led emergency medical services provision or to other supraglottic airway devices, which may have different characteristics. However, the principles underpinning the insertion and function of all supraglottic airway devices are similar.

In keeping with similar studies, our trial had relatively few survivors from which to gather longer-term outcomes. Furthermore, we were reliant on active patient consent and co-operation at both 3 and 6 months to collect the required modified Rankin Scale and EuroQol-5 Dimensions, five-level version, data. Despite considerable effort by the research teams, only 52.4% of survivors consented to active follow-up. Consequently, our analyses are affected by missing data with limited power and the risk of attrition bias. However, the proportions of missing data were very similar in the two groups, and there is no evidence that the availability of follow-up data was influenced by patient allocation. Furthermore, the sensitivity analyses did not alter our findings to any significant degree.

Future work

The Pragmatic Airway Resuscitation Trial (PART), published at the same time as this trial, compared another supraglottic airway device (the laryngeal tube) with tracheal intubation and reported 72-hour survival as the primary outcome, with different findings. Given that we have collected 72-hour survival in the AIRWAYS-2 trial, we are collaborating to undertake an individual patient meta-analysis.

We feel that an area of interest for a future trial would be exploration of alternative supraglottic airway device types compared with tracheal intubation, i-gel or an alternative advanced airway management strategy. Another area of interest would be a randomised trial of bag mask ventilation, use of which is widespread in countries where paramedics are not trained to provide tracheal intubation, compared with a supraglottic airway device.

There is also scope for similar research in other patient populations suffering cardiac arrest, including children, people with trauma and people in hospital.

Conclusions

The AIRWAYS-2 trial conducted successful and ethical research in critically ill patients who lacked capacity and required immediate life-saving treatment.

Among patients with out-of-hospital cardiac arrest, randomisation to a strategy of advanced airway management with i-gel compared with tracheal intubation resulted in no difference in favourable functional outcome at 30 days.

Longer term follow-up confirmed the results of the primary analysis. There were no significant differences in modified Rankin Scale score or the EuroQol-5 Dimensions, five-level version, between the i-gel and tracheal intubation groups at 3 and 6 months after out-of-hospital cardiac arrest.

In terms of the economic component of the trial, we conclude that there is no evidence to suggest a difference between the two groups.

Trial registration

The trial is registered as ISRCTN08256118.

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This report

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