GUIDELINES AND THE ADOPTION OF ‘LIPID RESCUE’ THERAPY FOR LOCAL ANAESTHETIC TOXICITY

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SUMMARY

Gathering evidence from animal experiments, an editorial in this journal and published human case reports culminated in the Association of Anaesthetists of Great Britain and Ireland recommending in August 2007 that lipid emulsion be immediately available to all patients being given potentially cardiotoxic doses of local anaesthetic drugs. This development offered an opportunity to track the adoption of an innovation by anaesthetists in the UK and to gauge the effects of guidelines. Two surveys, each of 66 NHS hospitals delivering acute care within London and its penumbra, examined the adoption of lipid emulsion therapy. After the publication of the editorial in autumn 2006, the spread of ‘lipid rescue’ was rapid. The timing of the adoption and the impetus for innovation varied substantially between the sampled hospitals. When the formal guidelines were published, approximately half the hospitals surveyed did not have lipid rescue. Of those that subsequently adopted it, half attributed their decision to the guidelines. At the end of 2007, there remained a small number of hospitals that had yet to adopt lipid rescue. Lipid rescue’s adoption by anaesthetists in the UK offers a rare example of swift adoption of an innovation. National guidelines accelerated the adoption of innovation by some hospitals.

RUNNING HEAD

Guidelines and innovation
The first account of lipid emulsion’s effectiveness in resuscitation from local anaesthetic overdose appeared in 1998, reporting its successful use in rats [1]. A further similar paper reporting successful results in dogs appeared in 2003 [2]. This was followed in 2004 by publication of a suggested treatment regimen for local anaesthetic-induced cardiac arrest in humans using lipid emulsion, dubbed “lipid rescue” [3]. An editorial in this journal in 2006 highlighted its probable efficacy in human beings and pointed out that ethically acceptable, randomised, controlled trials of lipid rescue in humans would be impossible [4]. The editorial concluded that where patients had not responded to conventional resuscitation after cardiac arrest attributable to local anaesthetic intoxication, lipid rescue should be considered – indeed that there was nothing to gain in withholding it, given the otherwise grim prognosis. In the same year, the first peer-reviewed accounts of lipid rescue’s effectiveness in local anaesthetic-induced cardiac arrest in humans appeared [5,6]. In each of the two cases, administration of lipid rescue was associated with restoration of effective cardiac output and both patients were discharged home neurologically intact.

In August 2007, the Association of Anaesthetists of Great Britain & Ireland (AAGBI) published guidelines recommending lipid rescue for the treatment of local anaesthetic toxicity and recommended that all departments administering potentially toxic doses of local anaesthetic should keep lipid emulsion immediately available [7].

We conducted two surveys of 66 National Health Service hospitals in London and its penumbra: one after the publication of the editorial but before the production of the guideline, and a second after the publication and widespread dissemination of the guideline. Our aim was to describe the uptake of the concept of lipid rescue in these hospitals and to try to correlate it with the various publications.
METHODS

We conducted surveys in two periods: October 2006 - December 2006 and October 2007 - January 2008. For each survey we contacted local representatives (College Tutors) of the Royal College of Anaesthetists in the 66 National Health Service (NHS) hospitals within contiguous areas of London and its suburbs, serving a population well in excess of 12 million. Each College Tutor was contacted by email and was asked to complete a survey on a website (www.surveymonkey.com). If the survey remained unanswered, the College Tutor was contacted again electronically, and then by telephone. If a response could still not be obtained from a hospital’s College Tutor, we made telephone contact and accepted answers from a substantive consultant anaesthetist employed in that hospital.

The surveys used are detailed in Appendix A. In summary, we asked if hospitals had lipid emulsion immediately available to patients receiving potentially toxic doses of local anaesthetic. If the hospital did, we asked when it was introduced, whether it was introduced by anaesthetic department members acting collectively or by an individual, and what motivated its introduction. If the hospital did not yet have lipid rescue available, we then asked why not. In each case, we asked respondents to select from a list of answers.

If a hospital reported having lipid rescue in the first survey, the given reported date of its introduction was used in all further analysis, even if in the second survey another date was reported.
RESULTS

We received answers from 56/66 (82%) hospitals in the first survey, and 59/66 (89%) in the second. In the first survey, lipid rescue was available to patients receiving potentially toxic doses of local anaesthetic in only 12/56 (21%) responding hospitals. A year later the position had changed significantly: the proportion of hospitals with lipid rescue had increased to 51/59 (86%). Of the 12 hospitals with lipid rescue at the first survey, 10 (83%) had been motivated by fear of toxicity. The consultant body as a whole were deemed responsible for its introduction in four hospitals, while an individual was thought responsible in eight hospitals (67%).

In the 44 hospitals that did not have lipid rescue at the first survey, the reasons given were as follows:

- In 15 hospitals, no individual consultant had taken on the task of introducing lipid rescue and in another five no departmental decision had yet been taken.
- Applications to the local Drug and Therapeutics Committee were pending (or lipid rescue was to be introduced “soon”) in 13 hospitals.
- Three hospitals reported never giving potentially toxic doses of local anaesthetic.
- Two hospitals’ respondents were not aware of lipid rescue.
- Another two hospitals’ respondents suggested more evidence was necessary before lipid rescue should be introduced.
- One application to the local Drugs and Therapeutics Committee had been rejected.
- One anaesthetic department (in a busy general hospital) had formally decided not to adopt lipid rescue.
- One hospital’s respondent explained that lipid rescue had not been introduced because no toxicity had occurred in the hospital.

Thirty-nine hospitals introduced lipid rescue between the two surveys. Once again, individuals appeared to be responsible for many introductions of lipid rescue, with both individual consultants (n = 12; 31%) and department heads (n = 6; 15%) contributing. The proportion of introductions attributed to collective departmental decisions increased slightly to 20 (51%). One hospital’s pharmacy department instituted lipid rescue’s adoption.
In August 2007, when the AAGBI’s guidelines were published, 32 (54%) of hospitals did not have lipid rescue. However, by the second survey a few months later, 24 of them had introduced lipid rescue, with 11 out of these 24 (45%) citing the AAGBI guidelines as their motivation, and seven out of 24 (29%) citing fear of toxicity. At the time of the second survey, there remained eight hospitals (14%) that reported not having lipid rescue. The reasons given were as follows: four reported that an application to the local Drugs and Therapeutics Committee was pending; three reported that no individual consultant had taken on the task; in one department no decision had yet been taken. Figure 1 gives further detail, showing how this process occurred over time, and how it related to the appearance of publications.
DISCUSSION

We have tracked the introduction of a new treatment to a large sample of hospitals providing acute care in the UK. Although many clinical innovations are introduced to a hospital’s practice gradually, it is easier to ascribe a precise date to the introduction of lipid rescue as it coincides with the introduction of bags of lipid to the areas in a hospital in which local anaesthetic drugs are given in large doses. The two surveys were performed at the time of the rapid introduction of this therapy, and were timed so as to be conducted before and after the production of guidelines relevant to the treatment by an authoritative, national, professional body.

We chose to survey a large group of hospitals in a single contiguous area so that the risk of sampling from “islands” of non-typical practice was avoided [8]. Although survey data have weaknesses, we believe that all NHS hospitals within our sample area in which anaesthesia was being delivered were identified in the survey. In hospitals from which we received no response to the two email approaches to the College Tutor, we accepted telephone answers from an available consultant. This may have introduced a source of error although, conversely, to include only hospitals whose College Tutors replied would have introduced a different selection bias. However, we believe that accepting responses from consultants other than the College Tutor was reasonable; these telephone interviews certainly significantly increased our data return.

Some aspects of the spread of lipid rescue are clear. Firstly, lipid rescue has spread widely and fast in the geographical region we studied. The first published reports of its use in humans appeared in mid-2006; by December 2007 >80% of hospitals in our survey had adopted it. Our data are consistent with the work of Williamson et al, who found that by May 2007, lipid emulsion was readily available on 49% of labour wards in the UK [9]. Secondly, while the hospitals we studied are geographically close and are staffed by doctors with similar training, the adoption of lipid rescue has occurred in different ways in different hospitals. In many, a single enthusiast was able to introduce lipid rescue acting seemingly almost alone, yet in others such an enthusiast was thwarted by the local Drugs and Therapeutics Committee. In other hospitals it seems that the introduction of lipid rescue was a more widely supported initiative. Thirdly, the promulgation of the AAGBI’s guidelines was not followed by a stepwise increase in the number of hospitals with lipid rescue. In addition, only about a half of the hospitals adopting lipid rescue after the guidelines’ publication attributed its introduction to their publication. Many of the introductions within this group were attributed to “fear of intoxication”. Yet this alone cannot have sufficed - intoxication by local
anaesthetic has been feared since the introduction of local anaesthetics themselves. Fear of the intoxication may have been combined with knowledge of lipid rescue’s promise. The guidelines may therefore have contributed to lipid rescue’s spread in more than the documented 45% of the hospitals adopting the new treatment after their publication.

The prompt adoption of an innovation is conventionally attributed to clear superiority, compatibility with existing practice and low net entry costs [10]. Lipid rescue has not been (and most likely never will be) proven to be unquestionably superior to “orthodox” treatment for local anaesthetic intoxication in humans but the experiments on animals and human case reports are increasingly suggestive. Lipid emulsions are familiar to anaesthetists as the principal constituent of total parenteral nutrition and as the usual carrier for the induction agent propofol. More generally, existing working practices are consistent with its introduction: lipid emulsions were already in most hospital formularies and no one outside the acute hospital needed be involved. Furthermore, costs are minimal, as supplies can be returned to pharmacy for use in total parenteral nutrition as they approach expiry.

The appearance of the AAGBI guidelines so swiftly after the initial case reports’ publication may also have accelerated the adoption of lipid rescue. However, despite the two case reports, the guidelines, the simplicity of the innovation itself and the neutral costs, there remained a minority of hospitals in which lipid rescue was not available to patients. We speculate that doctors in these hospitals made a risk-benefit analysis and judged adoption of lipid rescue unnecessary in their particular circumstances. Studying these “slow adopters” would require carefully designed qualitative evaluation of motivations, but might particularly benefit patients’ care if it illuminates the barriers to innovation. The adoption of lipid rescue was driven by individuals in some hospitals and propelled by the combined will of departments in other hospitals. If this pattern is reproduced, it suggests that an innovation’s adoption is best encouraged by several means simultaneously: guidelines, editorials and scientific publications may all contribute to its spread and should be deployed together although not perhaps all at the same time.
FIGURE 1

Uptake of lipid rescue from January 2005 to January 2008 in the hospitals responding to the survey.

A: February 2006 – Anaesthesia editorial
B: July 2006 – First case report published
C: August 2006 – Second case report published
D: August 2007 – AAGBI Guidelines published
REFERENCES

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6. MA Rosenblatt, M Abel, GW Fischer, CJ Itzkovich, JB Eisenkraft Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. *Anaesthesia* 2006; **105**: 217-8.


APPENDIX A

Survey questionnaire

Question 1
Does your operating department, recovery area or labour ward keep a lipid rescue pack? (That is a supply of lipid emulsion (Intralipid®) immediately available to treat patients overcome by local anaesthetic toxicity).

Answers allowed: Yes, No.

If respondents answered "Yes", they were directed to Questions 2-4; if No, to Question 5.

Question 2
When was the lipid rescue pack introduced? (If you are not sure of the date, please indicate the month and year that most closely matches your immediate recollection).

Answers allowed: year and month.

Question 3
Who was responsible for the decision to adopt lipid emulsion?

Answers allowed: Department head, individual consultant, Consultant body, Pharmacy, Risk Management Team, Other (please specify), free text.

Question 4
What was the main reason for adopting lipid emulsion?

Answers allowed: Fear of local anaesthetic intoxication, (The AAGBI guidelines), Legal or insurance considerations, other (please specify), free text.

The option of "The AAGBI guidelines" was available only at the second survey
Question 5
You have just told us that your hospital doesn't have a lipid rescue pack. Is this because:

Answers allowed: A department decision has been taken not to introduce one; No single consultant has been inclined to take it on; An application to your local Drugs and Therapeutics Committee is pending; An application to your local drugs and therapeutics committee has been rejected; other (please specify), free text.