Implementing protocol-based therapy of continuous neuromuscular blockade provides cost minimization


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of nondepolarising neuromuscular blocking agents (pancuronium and vecuronium) in the treatment of critically ill patients. A protocol-based therapy of neuromuscular blockade was compared with an empiric approach.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients admitted to the intensive care unit (ICU) who required continuous neuromuscular blockade for at least 6 hours. The authors did not report any exclusion criteria.

Setting
The setting was secondary care. The study was conducted in the USA.

Dates to which data relate
The dates to which the effectiveness and resource use data related were not reported. The price year was not reported.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
Successive patients admitted to the ICU, who required continuous neuromuscular blockade for at least 6 hours, were eligible for inclusion. Twenty-nine patients were included in the control group (empiric therapy) and 17 in the intervention group (protocol-based therapy). The authors reported that a sample size of 30 patients provided a power of 0.8, which could show an hourly cost difference of Can$3.00 at a significance level of 0.05. No patients appear to have been excluded from the analysis, while none appear to have refused to participate.

Study design
This was a prospective, cohort, observational study that was conducted in a single centre. The effectiveness data and resource use for empiric therapy were collected for 9 months, while the data for protocol implementation were collected for 5 months. The authors reported that ICU staff were unaware of data being collected for the empiric therapy, but were aware and encouraged to record reasons for deviations from the protocol during the protocol-based therapy phase. The mean duration of follow-up was not reported. No loss to follow-up was reported. Two of the patients (one in each group) were only included in the cost analysis.

Analysis of effectiveness
It was not stated whether the analysis of the clinical study was conducted on the basis of intention to treat, or on treatment completers only. The authors collected data on the duration of neuromuscular blockade and on protocol adherence. Protocol adherence was defined as the use of vecuronium (neuromuscular blocker) for patients with renal dysfunction, hepatic dysfunction or haemodynamic instability, and pancuronium (another neuromuscular blocker) for all other patients. Data were also collected on:

the doses of neuromuscular blockade,
the time to achieve blockade, and
the presence of excessive or inadequate blockade, and
the time from discontinuation of neuromuscular blockade to the first spontaneous movement in hours.

Both patient groups were reported to be similar in terms of the demographic data, ICU admission criteria, APACHE II scores, duration of mechanical ventilation, and length of ICU stay.

Effectiveness results
The duration of neuromuscular blockade was similar between the groups. There were no significant differences in terms of excessive or inadequate neuromuscular blockade.

The protocol adherence rate was 76.5%.

In the intervention group, the initial agent prescribed was pancuronium for 41.2% of the patients, (p<0.05 versus empiric therapy) and vecuronium for 58.8%.

The time to achieve adequate blockade and the time from discontinuation of neuromuscular blockade to the first spontaneous movement were not significantly different between the two groups. On the other hand, adequate neuromuscular blockade was reported to be higher with protocol-based therapy (52.3%) than with empiric therapy (32.7%), (p<0.05).

Clinical conclusions
With a relatively high protocol adherence rate, pancuronium was used significantly more often in the protocol group than the empiric group. With the exception of adequate neuromuscular blockade, which was higher in the protocol-based group, there were no statistically significant differences between the two approaches.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis. In effect, a cost-consequence analysis was performed.

Direct costs
The study perspective was not stated but only the costs to the health service were considered, including the total hospital acquisition cost for neuromuscular blocking agents. This cost was calculated as the sum of the costs of the individual
agents, then divided by the duration of the administration of neuromuscular blockade in order to obtain an hourly hospital acquisition cost. Resource use consisted of the total drug use and was recorded prospectively in the study. The quantities and the costs of the agents were derived using actual data, taken from the study centre, and reported separately. Discounting was not performed since the follow-up was less than one year. No extrapolation beyond this point was performed. The price year was not reported.

Statistical analysis of costs
The data were treated stochastically. Means and standard deviations (SDs) were provided for each estimate and statistical tests of significance were used. Student’s t-test and the Mann-Whitney U-test were performed.

Indirect Costs
No indirect costs were included in the analysis.

Currency
Canadian dollars (Can$).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The total cost in the protocol-based group was Can$79.03 (SD=514.75). This was not statistically different from the total cost in the empiric group Can$608.38 (SD=898.403). On the other hand, the mean hourly cost of neuromuscular blockade was Can$9.03 (SD=7.03) in the empiric group and Can$5.11 (SD=4.76) in the protocol-based group. This difference was statistically significant, (p<0.05).

Synthesis of costs and benefits
The costs and benefits were not combined as, in effect, a cost-consequences analysis was performed.

Authors’ conclusions
The protocol-based approach decreased the cost of therapy whilst enhancing the control of neuromuscular blockade and possibly promoting continuity of care by standardising patient therapy. However, the protocols were institution-specific and should be revised as new evidence becomes available.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. An empiric approach was the current practice in the centre and among other institutions. However, it was not stated whether neuromuscular blocking agents were the only relevant alternatives in the treatment of these critically ill patients. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a prospective cohort study, which was not the most appropriate design for the study question because of the risk of biases and confounding factors. A randomised clinical trial would have been the most appropriate
design to handle a study of this type. The authors acknowledged this limitation. However, they did not report any statistical analyses to account for potential biases or confounding factors. The authors reported that successive patients from the study population were eligible, but they did not clarify whether successive patients were enrolled. Thus, it would seem that the study sample was representative of the study population, but it is difficult to be certain. Both patient groups were shown to be comparable at analysis. The health outcomes analysed in the study were not presented clearly, which made it difficult to separate the primary from the secondary outcomes. The nature of the study represents a limitation to the internal validity.

**Validity of estimate of measure of benefit**
No summary health benefit was used. In effect, a cost-consequences analysis was conducted.

**Validity of estimate of costs**
The perspective of the study was not stated. The cost analysis included only those health care costs related to the purchase of pharmaceuticals. The costs and the quantities were reported separately which will enhance generalisability to other settings. However, relevant costs (ICU length of stay, drug administration-related costs such as consumables and staff, overheads and protocol training) were omitted from the analysis, but the authors provided no justification for their omission. Consequently, the true costs of the protocol-based approach might have been underestimated. It was not reported whether a cost-to-charge mechanism was used in the study. A statistical analysis of the costs was performed. However, the price year was not reported, which will make reflation exercises difficult.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies, finding their results to be consistent. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively. In addition, they acknowledged several limitations to their study. First, the study sample was small. Second, it was not a randomised controlled trial. Finally, the protocol development during the empiric phase might have changed in practice.

**Implications of the study**
The authors recommended the adaptation and implementation of their protocol at other institutions, and the subsequent revision of the protocol as new evidence becomes available.

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**MeSH**
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