Cardiovascular Topics

Economic evaluation of low-molecular-weight heparin in the management of patients with unstable coronary artery disease

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Summary

Objective. To undertake an economic evaluation of the administration and monitoring costs of the two different forms of heparin in patients with unstable coronary artery disease (UCAD).

Study design. Equivalent efficacy was found for low-molecular-weight heparin (LMWH) and for unfractionated heparin (UFH) in the treatment of patients with UCAD. Cost minimisation analysis was carried out according to current local clinical practice in both the public sector and the private sector hospitals. Cost identification was carried out using local cost information, collected separately in both settings, and included costs for wastage and re-siting of drips.

Perspective. For the public sector perspective was that of the health care provider and for the private sector that of the third-party payer.

Results. Public sector costs for 48 hours and 72 hours of UFH therapy were R330.21 and R471.06, respectively. In contrast costs of 4, 5 and 6 days of LMWH were R211.70, R252.28 and R294.94, respectively. Savings for 5 days of LMWH therapy versus 48 hours and 72 hours of UFH therapy were R77.41 and R77.93 per patient, respectively.

Private sector costs for 48 hours and 72 hours of UFH therapy were R761.14 and R1 022.58, respectively. In contrast costs of 4, 5 and 6 days of LMWH were R462.26, R545.86 and R629.46, respectively. Savings for 5 days of LMWH therapy versus 48 hours and 72 hours of UFH therapy were R215.28 and R476.72 per patient, respectively. Sensitivity analysis showed LMWH to be the most cost-efficient form of intervention.

Conclusion. The results were robust in both settings, showing that LMWH is the most cost-effective form of heparin therapy in this patient group.

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Unfractionated heparin (UFH) in combination with aspirin is used in the treatment of unstable coronary artery disease (UCAD).[1] However, UFH has a number of drawbacks, principal among which is the need for repeated laboratory monitoring to maintain a constant and predictable anticoagulant effect. Low-molecular-weight heparin (LMWH) has been shown to be as effective as UFH in the treatment of UCAD (FRIC study)[2] and to have pharmacological and pharmacokinetic advantages over UFH that include a predictable pharmacokinetic profile, high bio-availability and a long plasma half-life, all of which result in effective levels of

anticoagulant activity following subcutaneous (SC) administration and without the need for laboratory monitoring. The difference in monitoring requirements and the fact that LMWH is administered via the SC route as opposed to the intravenous (IV) route, indicate that cost of treatment will differ between the alternative forms of therapy. A full economic evaluation of the alternative forms of heparin was therefore carried out. Conduct and reporting of the economic evaluation was according to published guidelines.[3] The recommendations for restriction of bias in the conduct and reporting of economic evaluations sponsored by pharmaceutical companies[4] were adhered to at all stages of the study.

Methods

Study design

The results of the FRIC[2] study showed that the use of UFH or LMWH had similar results in the acute phase, and the use of placebo or LMWH during a subsequent prolonged treatment phase also had similar results. As the use of LMWH conferred no additional benefit to the patients in the prolonged treatment phase it was concluded that it would not be used in routine clinical practice, and the cost minimisation analysis (CMA) was therefore restricted to its use in acute therapy.

All patients also received aspirin, and since this aspect of the therapy was the same for both groups of patients it was not included in the cost analysis. It was found that current clinical practice in the Gauteng province of South Africa slightly differed from the clinical practice described in the FRIC[2] study. However, it was decided that the two were sufficiently similar to assume the same outcome equivalence for both alternative forms of heparin in this patient group.

Perspective

The perspective for the analysis in the public sector was that of the health care provider, whereas in the private sector it was that of the third-party payer.

Setting

The economic evaluation was carried out according to current local clinical practice in both the public and the private sector hospitals. Cost identification was carried out using local cost information, which was collected separately in both settings, as it was clear that unit costs would differ significantly between the two sectors.

Current clinical practice in the public sector

All patients arriving at accident and emergency units with unstable angina would have a drip sited by a professional nurse (nursing sister) and be given a bolus injection of 10 000 IU UFH. This was estimated to take 20 minutes of nursing time for preparation and administration. The majority of patients (90%) would be transferred to a cardiology ward and either receive a continuous intravenous infusion of UFH, 1 000 IU per hour for 48 - 72 hours, or 4 - 6 days (average 5 days) of LMWH by subcutaneous injection twice daily. It was estimated that administration of SC injections in pre-filled syringes would be carried out by a professional nurse and take 1 minute on each occasion.

For those receiving UFH a sterile 200 ml saline bag would be made up with 6 000 IU UFH and changed on a 6-hourly basis by a nursing sister, taking 10 minutes on each occasion. Each occasion would entail the use of a syringe and two needles to draw up the heparin and introduce it into the saline. For patients receiving 48 hours of therapy the heparin solution would be prepared on 8 occasions, and for those in 72 hours of therapy it would be prepared on 12 occasions. It was assumed that unused portions of UFH vials would be stored at 4°C and used on subsequent occasions (a conservative assumption assuming no wastage).

It was estimated that a drip would need to be re-sited on one occasion in 25% of all patients receiving 48 - 72 hours of continuous infusion therapy. The process of re-siting would entail the disposal of the IV infusion set and the replacement of all consumables associated with the infusion. It was estimated that this process would take 30 minutes of professional nurse time.

Monitoring of partial thromboplastin time (PTT) is required when giving UFH in order to maintain the correct dosage.[5] Monitoring is not required in patients receiving LMWH.[5] For PTT monitoring a clinician would take a blood sample and later retrieve and interpret the results. It was estimated that this process would entail the use of a Vacutainer, needle and swab, and 10 minutes of time on each occasion. The costs of the disposables were not included in the cost analysis as they are incorporated in the laboratory cost. Patients would be monitored for PTT twice daily (morning and afternoon), so those on 48 hours' therapy would be monitored on 4 occasions, and those on 72 hours' therapy on 6 occasions.

Current clinical practice in the private sector

Many similarities with the public sector exist, except that all patients in the private sector would be admitted to the coronary care unit from accident and emergency units as opposed to a cardiology ward. One implication of this setting is that monitoring of PTT would be carried out more frequently. It was assumed that patients in the private sector would be monitored on 6 occasions in 48 hours, and on 8 occasions in 72 hours. Blood samples for monitoring would be taken from the laboratory by a phlebotomist. Charges are made for the collection of materials and for specimen handling on each occasion (in addition to the charge for the PTT test).

Another difference is that in the private sector unused portions of UFH vials would not be stored and used at a later stage but discarded, so the cost of a whole vial of UFH 5 ml 1 000 IU/ml was used for calculation each time a new saline bag was prepared.

It was estimated that a drip would need to be re-sited on

one occasion in 25% of all patients receiving 48 - 72 hours of continuous infusion therapy. The process of re-siting would entail the disposal of the IV infusion set and the replacement of all consumables associated with the infusion. It was noted that this procedure would incur a 'physician fee for insertion of an IV cannula'.

No separate charge would be made for nursing procedures, as nurse provision is included in the ward fees and would be the same for all patients staying in the same ward for the same period of time.

Factors common to both settings

Wastage of IV material has been reported to be high in other institutions,[6] ranging from 2.06% to 19.98%. It was decided to use a conservative figure of 10% in this study. Side-effects of IV therapy include thrombophlebitis, infection and local sepsis, which are not normally treated actively but resolve in time, so no cost is associated with them. The length of stay in hospital for patients is the same irrespective of whether they receive UFH or LMWH, so the inpatient hospital costs have not been included in the cost calculations.

Identification of costs

Unit costs were obtained in the public sector from various departments of Johannesburg Hospital: pharmacy purchasing, special dispensary, cardiology wards, hospital administration, and the South African Institute of Medical Research (SAIMR) for laboratory costs. Unit costs were obtained in the private sector from MedManage Johannesburg, the Representative Association of Medical Schemes, and various private hospital pharmacies.

TABLE I. UNIT COSTS FOR LMWH, UFH, IV INFUSION SET AND THE REPLACEMENT OF ALL CONSUMABLES ASSOCIATED WITH THE INFUSION, LABORATORY TESTS, NURSING AND PHYSICIAN COSTS

	Unit cost (SA rands)	
Item	*Private sector*	*Public sector*
Jelco cannula	18.51	1.62
Webcol swab	0.23	0.05
Drip line	8.85	3.95
Dial-a-flow	43.11	8.70
IV Op-Site	11.75	1.23
200 ml saline	19.13	11.75
Bolus needles	0.45	0.12
Bolus syringe (2 ml)	1.28	0.20
Cont. inf. needles	0.45	0.12
Cont. inf. syringes	1.28	0.20
Bolus UFH (5 ml, 5 000 IU/ml)	24.55	6.47
Cont. inf. UFH (5 ml, 5 000 IU/ml)	24.55	6.47
Specimen handling fee	9.40	n/a
Collection material	5.10	n/a
Physician fee	25.30	7.60
PTT test	24.50	21.96
Fragmin 5 000 IU/0.2 ml PFS	41.57	20.35
10% wastage (UFH)/cycle	12.79	3.70
IV re-siting (25% pts/cycle)	38.29	13.93
IV A & E siting (for LMWH pts)	127.86	45.22

PFS = pre-filled syringe; A & E = accident and emergency.

Results

Unit costs in both the public and private sector hospitals for LMWH, UFH, IV infusion sets and the replacement of all consumables associated with the infusion, laboratory tests, nursing and physician costs are shown in Table I.

A cost of R4.10 per 10 minutes was applied to nurses' time in the public sector, whereas a zero cost was applied in the private sector as nursing costs are factored into ward charges and all patients are assumed to have equal periods of stay and thus equal ward charges.

Table II shows the costs to the provider hospital in the public sector for UFH IV therapy for 48 hours and 72 hours, respectively, in comparison with LMWH SC therapy for 4, 5 and 6 days, respectively.

TABLE II. PUBLIC SECTOR COSTS (TO THE PROVIDER HOSPITAL) FOR UFH AND LMWH THERAPY

Therapy	*Cost per patient (SA rands)*
48 h UFH IV	330.21
72 h UFH IV	471.06
4 d LMWH SC	211.70
5 d LMWH SC	252.28
6 d LMWH SC	294.94

The potential savings for 5 days of LMWH therapy versus 48 hours and 72 hours of UFH therapy were R77.41 and R77.93 per patient, reducing costs by 23% and 24%, respectively.

Table III shows the costs to the third-party payer in the private sector for UFH IV therapy for 48 hours and 72 hours, respectively, in comparison with LMWH SC therapy for 4, 5 and 6 days, respectively.

TABLE III. PRIVATE SECTOR (TO THE THIRD-PARTY PAYER, EXCLUDING WARD COSTS) FOR UFH AND LMWH THERAPY

Therapy	*Cost per patient (SA rands)*
48 h UFH IV	761.14
72 h UFH IV	1 022.58
4 d LMWH SC	462.26
5 d LMWH SC	545.86
6 d LMWH SC	629.46

The potential savings for 5 days of LMWH therapy versus 48 hours and 72 hours, of UFH therapy were R215.28 and R476.72 per patient, reducing costs by 28% and 47%, respectively.

Sensitivity analysis

The results were very robust in both settings, and even under the most extreme variations in sensitivity analysis showed LMWH to be the most cost-effective form of heparin therapy in this patient group.

If there was *no* wastage for UFH, and *no* re-siting of IV drips, *and* all consumable, staff and monitoring costs were reduced by 10%, then 48 hours of therapy with IV UFH would cost R281.32 in the public sector and R639.06 in the private sector. Under these conditions there is still a saving of R48.89 and R122.08 per patient in the public and private sectors, respectively.

If the total cost of 5 days of LMWH was increased by 10% to R277.51 in the public sector and R600.45 in the private sector, it is still the most cost-efficient form of intervention. This calculation includes the cost of setting up an IV drip and giving an initial bolus UFH injection to all patients, including those who later receive LMWH. Under these conditions there is still a saving of R52.70 and R160.69 per patient in the public and private sectors, respectively.

Discussion

This study has shown that LMWH is the cost-effective treatment of choice in this patient group in both the public sector and private sector settings in South Africa. A literature search did not reveal any other economic evaluations of LMWH versus UFH in unstable coronary artery disease, but some studies have been carried out in the use of the alternative heparin therapies for other indications such as the prophylaxis and treatment of deep-vein thrombosis.[5] These studies also concluded that LMWH was the more cost-effective alternative, mainly due to ease of administration and the fact that monitoring is not required.

An important factor that has not been taken into account is the discomfort and inconvenience associated with IV therapy for the patient, which is clearly negated by delivering LMWH via the SC route, making the use of LMWH considerably more appealing to the patient.

The time that is saved for staff working on the wards has been costed according to the salaries they earn; however, this greatly underestimates the true opportunity cost of the time taken to set up and maintain an IV infusion, and to monitor PTT levels. Time saved by giving LMWH as opposed to UFH may be used to care for other patients and to increase the quality of care, plus to increase the time that the caregiver has to make important clinical decisions and deliver high-quality health care to all patients.

It is clear that in both settings the most efficient form of therapy in this patient population is LMWH. Even under extreme variations in costs during sensitivity analysis, LMWH is shown to cost less than traditional UFH IV heparin. It is therefore recommended that for the management of patients with acute unstable angina or non-Q-wave myocardial infarction LMWH be given twice daily by SC injection for 4 - 6 days, as opposed to 48 hours or 72 hours of UFH via IV infusion.

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