POSTOPERATIVE CHANGES OF ERYTHROCYTE SEDIMENTATION RATE, PLASMA VISCOSITY AND C-REACTIVE PROTEIN LEVELS AFTER HIP SURGERY

B. OKAFOR [1], G. MACLELLAN [2]

We measured the behavior of the erythrocyte sedimentation rate (ESR), plasma viscosity (PV), and C-reactive protein (CRP) in 66 patients who underwent hip implant operations, from day 0 to day 21 postoperation. We analyzed the behavior of these parameters after the trauma of the operation. We identified a subset of patients with evidence of superficial clinical infection / inflammation, where the magnitude and duration of the response to surgery was different from the main group. PV and CRP show less variability between patients and consequently are better indicators of the acute phase response than the ESR which requires a series of values in order to demonstrate a trend. PV can be obtained simply and rapidly, which would make it a powerful tool in determining persistent inflammation.

Key words : hip surgery ; infection ; biochemistry.
Mots-clés : chirurgie de la hanche ; infection ; biochimie.

INTRODUCTION

There still exists controversy about the exact values of the erythrocyte sedimentation rate (ESR), plasma viscosity (PV) and C-reactive protein (CRP) in orthopedic practice with respect to their relative sensitivity and specificity as indicators of pathology. The role of ESR and CRP as markers of the acute phase response appears to be relatively well established (1, 2, 3, 4, 5, 7) as well as their ability to detect infection (9, 11). In contrast, the role of PV in orthopedic practice appears to be uncertain. Harris (6) observed that PV may be more sensitive than the ESR in the elderly population in detecting disease states since it showed less variability, in contrast to the multifactorial dependency of the ESR. Additionally the ESR has been found to be less informative in the context of infection and loosening (4, 10, 11). Nevertheless there appears to be a sparse amount of information in the literature comparing ESR, PV and CRP in the context of postoperative behavior and response to infection / inflammation. We therefore sought to examine the behavior of these parameters, at set intervals, after hip surgery.

MATERIALS AND METHODS

Seventy patients were recruited into the study prior to hip surgery requiring implant insertion ; they were followed up prospectively. All patients had a series of blood tests on admission and three weeks thereafter. Exclusion criteria were preoperative sepsis, malignancy, rheumatoid arthritides, connective tissue disease or immunosuppressive treatments. A total of four patients were excluded from the study. Thirty-three patients had total hip arthroplasties for degenerative arthritis. The remainder required either hemiarthroplasties or dynamic hip screw fixation for traumatic hip fractures (table I). Clinical evaluation prior to surgery included

Table I. — Clinical material

n = 66
Female : male = 47 : 19
Total hip replacement = 33
Dynamic hip screw = 14
Hemiarthroplasty = 19
Age range = 63-92 (mean 74 years)

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blood count, hematocrit, plasma viscosity, erythrocyte sedimentation rate, C-reactive protein, plain chest radiograph, urinanalysis, body temperature and impedance plethysmography in order to screen for lower limb thromboembolic disease. Clexane® low molecular-weight heparin and graduated compression stockings were used as antithromboembolic measures. Three doses of cefuroxime were administered perioperatively. All nonsteroidal antiinflammatory agents were discontinued prior to surgery. General anesthesia with epidural anaesthesia was used in the majority of cases ; intravenous fluids were continued for an average of 24 hours after the operation ; an average of 900 ml of whole blood was tranfused within 72 hours of the operation.

Routine daily clinical examination on all patients recorded temperature, pulse and cardiorespiratory status. Microbiological analysis of sputum, urine and wound discharge were performed ; wound discharge, if present, was recorded after removal of the surgical drains at 1 to 2 days postoperation. Blood tests for ESR, CRP, PV, leucocyte count and hematocrit were carried out on days 2, 7 and 21. Impedance plesthymography (to exclude deep vein thrombosis) and chest radiography (to exclude chest infection / atelectasis) were performed on day 7. An ESR above 20 mm/h and a PV above 1.7 cp, measured by the Coulter V2 Viscometer, were regarded as abnormal. The CRP g/dl was measured by initial latex screening followed by Beckman array nephrometry.

RESULTS

Eight patients were noted to have inflamed discharging wounds that were potentially infected. For record purposes these were denoted as "potentially infected" and were defined as those wounds where there was marked inflammation accompanied by seropurulent discharge, pyrexia and a leucocytosis. The infected group was subdivided into whether microbiology was positive or negative on the basis of growth after 48 hours isolation of the wound swabs, since we recognize that a sterile culture might be obtained as all patients had perioperative antibiotics. Blood cultures were also performed on all potentially infected cases, and all were negative. Clinical examinations and investigations did not reveal an additional source of sepsis or inflammation. Of the eight discharging wounds, two were found to grow low-grade Staphylococcus aureus ; the remaining six yielded negative growth. All potentially infected cases responded clinically to intravenous antibiotics with apparent resolution of wound inflammation / discharge. All patients were discharged at approximately 2 weeks without any deterioration in joint function or overall health and were followed up closely as outpatients for clinical review and blood tests. At 12 weeks three-phase technetium bone scans were performed on all potentially infected patients and were found to be normal.

a) **Behavior of plasma viscosity**

Table II and figure 1 illustrate the behavior of PV ; in the normal group a peak of 1.77 cp occurred within 48 hours, followed by a steady decline beyond the three-week period. Kruskal-Wallis

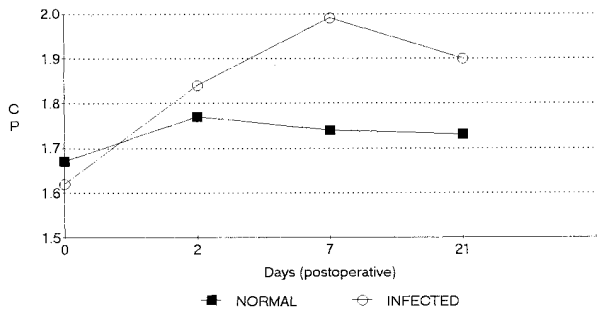

Fig. 1. — Variation of plasma viscosity with time in the normal and "infected" groups.

Table II. — Plasma viscosity distribution mean values (centipoise, cp)

	day 0	day 2	day 7	day 21
normal	1.67 (0.01)	1.77 (0.02)	1.74 (0.02)	1.72 (0.02)
infected	1.62 (0.04)	1.84 (0.05)	1.99 (0.05)	1.89 (0.04)

( ) = standard error of the mean.

analysis of variance was significant, with a p value of 0.0005 denoting that variations within the columns in table II are significantly greater than expected by chance. Dunn's multiple post-test comparisons demonstrated significant differences between the mean values of day 0 versus day 7 but not day 0 versus day 21 : in other words, by day 21 the PV in the normal group had normalized.

In the infected subset, the magnitude and duration of the PV response was significantly greater than in the normal group (table II and fig. 1). Analysis of variance gave a p value of < 0.0001 with the most significant variation in the mean result occurring between day 0 and day 2 values, which reflected the steep rise occuring during the first 48 hours, peaking at day 7 and followed by a gradual decline.

b) Erythrocyte sedimentation rate behavior

The acute rise and decline of the ESR almost paralleled the behavior of PV, with a steeper rise and fall in the infected subset (table III and fig. 2). In the normal group the variations were significantly different for day 0 versus day 2 and day 0 versus day 7, but not for day 0 versus day 21. This reflected the process of normalization of ESR by day 21 in the normal population. In the infected group the postoperative values of ESR were significantly different from the day 0 value, reflecting the persistent inflammatory state.

c) C-reactive protein behavior

CRP rose and peaked at a mean of 0.146 g/dl at day 2 in the normal group ; by day 21 it had normalized to a value of 0.028 g/dl (table IV and fig. 3). With respect to the infected subset the CRP also peaked at day 2 and then showed a persistent elevation on day 7 and day 21 (table IV). Analysis

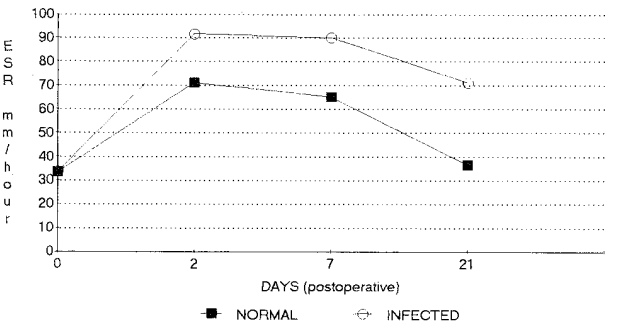

Fig. 2. — Variation of erythrocyte sedimentation rate with time in the normal and "infected" groups.

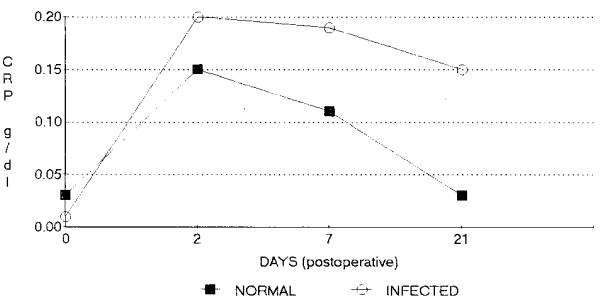

Fig. 3. — Variation of C-reactive protein with time in the normal and "infected" groups.

Table III. — Erythrocyte sedimentation rate distribution mean values (mm/h)

	day 0	day 2	day 7	day 21
normal	33.6 (2.6)	71 (3.6)	65 (4.6)	36.5 (5.2)
infected	33.8 (5.1)	91.6 (4.6)	90.1 (3.5)	71.2 (4.1)

( ) = standard error of the mean

Table IV. — C-reactive protein distribution mean values (g/dL)

	day 0	day 2	day 7	day 21
normal	0.03 (0.01)	0.15 (0.01)	0.11 (0.01)	0.03 (0.01)
infected	0.01 (0.01)	0.2 (0.03)	0.19 (0.03)	0.15 (0.02)

( ) = standard error of the mean

of variance gave a p value of less than 0.001 for both the main group and the infected subset. Dunn's multiple post-test comparison for both groups was also significant, particularly for day 0 versus day 21 CRP values for the infected subset.

The unpaired t test was used to determine whether there was a significant difference between the mean values of the normal and the infected groups for each parameter (ESR, CRP, PV). The two-tailed p values were less than 0.0002 for all three parameters respectively, suggesting that continued elevation of all 3 parameters in the infected subset was abnormal and significantly different from the normal group.

No correlation was found between the magnitude of the responses of the three parameters and sex, age, operation time, amount of bleeding and requirement for blood transfusion.

DISCUSSION

At 25° C the normal plasma viscosity ranges from 1.50 to 1.72 cp (1, 2, 5, 6, 8). The magnitude of its value is largely dependent on proteins, especially globulins and fibrinogen. ESR depends on rouleaux formation which in turn depends on age, plasma proteins, hematocrit, red and blood cell flow rate. Harris (6) showed that ESR values had a notable distribution in the elderly population : 28% had an ESR of 0 to 7 mm/h, 56% had values of 8 to 20 mm/h and 26% had above 20 mm/h.

There is a closer correlation between plasma protein levels and PV, and consequently PV measurement is a sensitive indicator of plasma protein response to inflammation and tissue damage (2, 5, 6, 8). Unpredictable variations in the ESR, due to multiple factors, are avoided. The plasma may be kept for over 24 hours, whereas the ESR must be measured within six hours of blood sampling. The PV can be determined by using a simple viscometer. Results with a coefficient of variation of less than 1% can be obtained, with each test taking less than 2 minutes to perform compared to one hour required for ESR estimation.

CRP is one of the acute phase proteins ; it is the first to rise and fall during a metabolic response and in the normal quiet state the CRP should be undetectable. This temporal behavior of the acute phase reactants is independent of age, sex, anatomical location of the surgery, and whether the surgery is elective or trauma. The role of ESR and CRP in surgery appears to be well established, particularly with regard to infection screening and monitoring (7, 9, 10, 11). The role of PV in orthopedic surgery is less well established. It provides a simple and reliable way of monitoring changes in the plasma protein levels as a result of trauma, inflammation, or infection. It has the added advantage that the result is available after 2 minutes when performed on stored blood (for up to 24 hours).

Analysis of the results shows that the variations in the mean values for both the main group and the infected subset were significant. ESR and PV variations were significantly greater than those expected by chance. After day 7 ESR and PV responses were no longer significantly different from day 0 in the main group (normalization had occurred between day 7 and 21) ; in contrast, the data would suggest that CRP normalization occurred later (approximately 3 weeks in the main group). In the "infected / inflamed" group it would appear that continued CRP elevation by the third week was indicative of persistent sepsis / inflammation, whereas for PV repeated elevated values between day 7 and 21 suggest inflammation. This temporal relationship is important because it allows one to determine when to perform these tests after surgery, and to decide when they are significantly abnormal. For the detection of early infection / persistent inflammation, we would recommend repeat blood tests between day 7 and day 21 postoperation. The multifactorial dependency of the ESR reduces its reliability in this clinical setting, and elevated values should be interpreted with caution unless there is a reference preoperative or day 0 value available, whereas PV and CRP are better tools as they show less variability. The simplicity and speed of PV measurement over CRP, in practical terms, means that results are immediately available, and appropriate treatment can be commenced. The CRP, on the other hand, can be used to support the PV results if there is any doubt.

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RÉSUMÉ

B. OKAFOR, G. MACLELLAN. Modifications post-opératoires de la vitesse de sédimentation des hématies, de la viscosité plasmatique et du taux de C-reactive protein après chirurgie de la hanche.

Les auteurs ont étudié le comportement de la vitesse de sédimentation des hématies (VS), de la viscosité plasmatique (VP) et de la C-reactive protein (CRP) chez 66 patients soumis à des opérations sur la hanche avec mise en place d'un implant, pendant les 21 premiers jours suivant l'opération. Ils ont identifié un sous-groupe de patients qui a présenté des signes cliniques d'infection ou d'inflammation superficielle et qui se distinguait de l'ensemble du groupe par l'importance et la durée des modifications observées. La VP et la CRP font preuve d'une moindre variabilité entre patients et sont par conséquent de meilleurs indicateurs de la réponse en phase aiguë que la VS qui requiert une série de valeurs successives pour démontrer une tendance. La viscosité plasmatique peut être obtenue de facon simple et rapide, ce qui devrait en faire un outil intéressant pour objectiver la persistence d'un état inflammatoire.

SAMENVATTING

B. OKAFOR, G. MACLELLAN. Postoperatieve wijzigingen van de sedimentatiesnelheid, de plasmaviscositeit en de C-reactieve eiwitten na heupchirurgie.

De auteurs hebben het gedrag van de sedimentatiesnelheid (SS), de plasmaviscositeit (PV) en de C-reactieve eiwitten (CRP) bij 66 patiënten na een heupoperatie onderzocht. Dit wed gevolgd gedurende de eerste 21 dagen postoperatief. Zij onderscheidden een subgroep van patiënten met klinische tekens van infectie op oppervlakkige inflammatie en die zich eveneens onderscheidden van de gans groep door belangrijke en langdurige modificaties biochemisch.
De PV en CRP vertonen minder variabiliteit tussen de patiënten en zijn bijgevolg de beste indicators op de acute fase, dit ten opzichte van de sedimentatiesnelheid. De PV kan worden bekomen op een snelle en eenvoudige wijze en dit is een interessant werktuig om de blijvende inflammatoire reactie postoperatief te objectiveren.