International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2020; 6(3): 934-937

www.orthopaper.com
Received: 18-05-2020
Accepted: 21-06-2020

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Effects of reamed intramedullary nailing on altered body temperature, CRP and plasma lactate

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DOI: https://doi.org/10.22271/ortho.2020.v6.i3n.2305

Abstract
Congenital metabolic disorders include type I glycogen storage disease. Examples of drugs/toxins which give rise to elevated lactate are methanol, ethanol, epinephrine and acetaminophen. L-lactate levels in CSF will generally mirror those in blood/plasma. However, increased lactate levels in CSF in the absence of increased blood/plasma lactate concentration have been reported in cases of bacterial meningitis, cerebral hypoxia, ischemia and in certain inborn errors of metabolism e.g. pyruvate dehydrogenase deficiency, mitochondrial myopathies and biotinidase deficiency. Patients with additional injuries or pre-existing known severe pathologic problem (such as malignancy, active infectious disease, rheumatoid disease) were excluded from the study. Fourty patients (32 males; 8 females; mean age, 43.1 (range, 20–97) years) who sustained isolated closed diaphyseal fracture of the femur or the tibia remained in the study group. All femoral fractures and tibial fractures were treated with an interlocking nail, with reamed technique. The value of plasma lactate pre operatively was 15.3. On the 1st POD, the mean value was 14.8 ($p = 0.849$), and on the 3rd POD it was 14.3. And on the 10th POD plasma lactate value was 15.3 in the control group almost similar to the preoperative mean value.

Keywords: Reamed intramedullary nailing, body temperature, CRP

Introduction
L-lactate is the end product of anaerobic glycolysis. It is derived predominantly from white skeletal muscle, brain, skin, renal medulla and erythrocytes. Lactate dehydrogenase catalyses the reduction of pyruvate to lactate.
There are two major clinical settings in which lactic acidosis occur:

- Conditions associated with hypoxia e.g. shock, congestive heart failure, myocardial infarction, blood loss and pulmonary edema.
- Metabolic or drug/toxin related disorders. Examples of metabolic disorders include diabetes mellitus, hepatic disease and neoplasia.

Congenital metabolic disorders include type I glycogen storage disease. Examples of drugs/toxins which give rise to elevated lactate are methanol, ethanol, epinephrine and acetaminophen.
L-lactate levels in CSF will generally mirror those in blood/plasma. However, increased lactate levels in CSF in the absence of increased blood/plasma lactate concentration have been reported in cases of bacterial meningitis, cerebral hypoxia, ischemia and in certain inborn errors of metabolism e.g. pyruvate dehydrogenase deficiency, mitochondrial myopathies and biotinidase deficiency.
In 2005, Christos Garnavos, Stamatia-Tina Xirou, Andreas Nikolatos, Nikolaos Kanakaris *et al*. stated that reamed intramedullary nailing causes an acute elevation of body temperature as well as significant alteration of both ESR and CRP.
This inflammatory reaction can last for several days postoperatively. Persistently, the temperature was elevated in the evening, could be easily controlled by simple oral medication, and did not influence patients' general condition, mobilization, and rehabilitation program.
The diagnostic value of the ESR and CRP may not be useful in the early postoperative period after reamed intramedullary nailing for the investigation of complications, such as infection [1].

P. V. Giannoudis, *et al.* stated that an inflammatory process has been implicated in the pathogenesis of the Adult Respiratory Distress Syndrome (ARDS) and Multiple Organ Failure (MOF) where an initial insult (the first hit) or subsequent insults (second hit) create a Systemic Inflammatory Response Syndrome (SIRS) which leads to end organ damage.

It has been suggested that nailing of the femur is a significant insult (second hit) in some trauma patients and should be avoided. And concluded that study shows that there is a second hit associated with femoral nailing and suggests that an unreamed technique may be less stimulating [2].

Crowl *et al.* reported that occult hypoperfusion, defined as a serum lactate >2.5 mmol/L, before early reamed IMN of a femoral shaft fracture was associated with increased complications.

Conclusions from this investigation were that patients with a femoral shaft fracture and a lactate $\geq$ 2.5 mmol/L should undergo definitive fixation when lactate is corrected in 1997 Bosse MJ, MacKenzie EJ, Riemer BL, *et al.* stated that Their study does not support the hypothesis that intramedullary nailing with reaming in multiply injured patients who have a thoracic injury potentiates the development of adult respiratory distress syndrome.

Other major or minor injuries, combinations of these injuries, therapeutic variations, patient-related variables, or bias in the selection of patients might account for the differences that have been reported for other series [3].

Justin E. Richards *et al.* concluded that Median admission lactate of 3.7 mmol/L was associated with duration of mechanical ventilation $\geq$5 days, whereas median preoperative lactate of 2.8 mmol/L was not, when multisystem trauma patients with a femoral shaft fracture were treated with reamed IMN within 24 hours after admission.

In 2002, Helttula *et al.* stated that there was unchanged cardiac performance but pathologically altered pulmonary vascular tone were unrelated to the type of nailing technique. Increased oxygen consumption was observed as well [4].

Methodology

All adult patients who sustained an isolated closed fracture of the femoral or tibial diaphysis, regardless of their gender, and degree of fracture comminution and who were treated with reamed intramedullary nailing, were included in this study (study group).

All adult patients who sustained isolated, closed, intertrochanteric fractures and who were treated with a Dynamic Hip Screw or Proximal Femoral Nailing, regardless of their gender, and degree of fracture comminution during the same period of time, constituted the control group.

Patients with additional injuries or pre-existing known severe pathologic problem (such as malignancy, active infectious disease, rheumatoid disease) were excluded from the study.

Fourty patients (32 males; 8 females; mean age, 43.1 (range, 20–97) years) who sustained isolated closed diaphyseal fracture of the femur or the tibia remained in the study group. All femoral fractures and tibial fractures were treated with an interlocking nail, with reamed technique.

After exclusions, 40 patients (30 males; 10 females; mean age, 60.09 (range, 28–85) years) remained in the control group. Their fractures were treated with a Dynamic Hip Screw or proximal femoral nail.

All patients received 3 doses of 3rd -generation cephalosporin (3 days postoperatively). They were all mobilized as soon as possible after the operation (1–3 days) using partial-to-full weight bearing, depending on stability of the fixation and patient's biologic status.

All patients remained in the hospital for at least 11 days postoperatively to have all blood tests and temperature measurements taken and evaluated in a similar manner and to be under close medical attention in case they developed any complications.

Body temperature was monitored every 6 hours by the nurse in charge in all patients in both the study and control groups during the study period. The highest temperature value for each day was taken and recorded.

ESR, and CRP were evaluated before the operation (up to 1–5 days from admission), immediately postoperatively (1 POD), and on day 3, and on day 10 after the operation.

During the postoperative period, all patients were under close supervision for early detection of initiation of a complication. Apart from the daily detailed clinical examination and changing of the wound dressings, they underwent the basic biochemical and urinary investigations on the 1st, 3rd, and 10th postoperative days.

Patients who remained in the study did not develop any significant problem throughout the study period.

Results

Table 1: Pre-operative

		N	Min	Max	Mean	SD	P Value
ESR	UR	40	10	141	55.1	33.5	0.153
	R	40	4	160	42.8	37.7	
CRP	UR	40	3	24	9.8	5.4	0.072
	R	40	3	24	13.1	4.9	
Plasma	UR	40	6.7	37.6	15.3	5.6	0.520
Lactate	R	40	5.4	3.0	14.5	4.8	
TEMP	UR	40	98.4	99.3	98.7	0.2	0.044
	R	40	98.0	99.1	98.6	0.2	

There is no statistically significant difference pre operatively for the parameters ESR, CRP, Plasma Lactate but there is a significant difference for the parameter Temperature between the 2 groups (Unreamed and Reamed)

Table 2: Post-operative Day 1

		N	Min	Max	Mean	SD	P Value
ESR	UR	40	15	150	67.5	35.6	0.929
	R	40	12	140	66.8	34.3	
CRP	UR	40	3	24	12.3	5.0	0.517
	R	40	3	24	13.1	4.9	
Plasma	UR	40	6.2	36.7	14.8	6	0.104
Lactate	R	40	6.3	23.9	12.7	4.5	
TEMP	UR	40	98.2	99.2	98.7	0.3	< 0.001
	R	40	98.6	102.5	100.6	1.1	

There is no statistically significant difference on POD 1 for the parameters ESR, CRP, Plasma Lactate, but there is a significant difference for the parameter Temperature between the 2 groups (Unreamed and Reamed)

Table 3: Post-operative Day2

		N	Min	Max	Mean	SD	P Value
ESR	UR	40	8	180	84.7	48.0	0.858
	R	40	17	165	82.7	45.1	
CRP	UR	40	3	24	11.8	3.9	0.355
	R	40	6	24	12.7	3.8	
Plasma	UR	40	5.4	33.9	14.3	5.3	0.384
Lactate	R	40	6	28.8	13.2	4.9	
Temp	UR	40	98.2	99.0	98.6	0.2	< 0.0001
	R	40	98.4	1.3	99.8	1.1	

There is no statistically significant difference on POD 3 for the parameters ESR, CRP, PLASMA LACTATE, but there is a significant difference for the parameter TEMPERATURE between the 2 groups (Unreamed and Reamed)

Table 4: Post-operative Day 10

		N	Min	S	Mean	SD	P Value
ESR	UR	40	12	170	72.9	42.9	0.466
	R	40	8	170	65.5	41.7	
CRP	UR	40	3	24	7.2	5.0	0.280
	R	40	3	12	6.0	4.2	
Plasma	UR	40	5.8	24.6	15.3	4.7	0.712
Lactate	R	40	7.3	42.0	14.8	6.1	
Temp	UR	40	98.2	99.7	98.6	0.1	0.248
	R	40	98.0	101.0	98.7	0.6	

There is no statistically significant difference on POD 10 for the parameters ESR,
CRP, PLASMA LACTATE, and TEMPERATURE

The CRP values followed a similar course as those of the ESR in the two groups. Pre operatively it was 12.8, POD 1 it was 13.1 and on the 3rd postoperative day to 12.7 ($P < 0.0001$ compared with the preoperative mean value). On the 10th postoperative day, CRP mean value had declined to 6.

The value of the CRP preoperatively was 9.8. On the 1st postoperative day, the mean value was 12.3 ($P < 0.0001$) and on the 3rd postoperative day was 11.8.

On the 10th postoperative day, CRP mean value was 7.2, almost similar to the preoperative mean value.

The plasma lactate values preoperatively were 14.5, POD 1 it was 12.7 and on 3rd POD it was 13.2. (p =0.248) on the 10th POD, plasma lacatate mean value was 14.8 in the study group, almost similar to the preoperative mean value.

The value of plasma lactate pre operatively was 15.3. On the 1st POD, the mean value was 14.8 (p = 0.849), and on the 3rd POD it was 14.3. And on the 10th POD plasma lactate value was 15.3 in the control group almost similar to the preoperative mean value.

Patients in the study group had an average body temperature of 98.6_F preoperatively. On the 1st postoperative day, the mean temperature rose to 100.6_F (*P*, <0.0001 compared with the preoperative mean value) and on the 3rd postoperative day decreased to 99.8_F (*P*, < 0.0001 compared with the preoperative mean value. On the 10th postoperative day, the mean temperature returned to normal level of 98.7.

Patients in the control group had a normal temperature preoperatively (98.7_F). Then experienced no change of body temperature on the first postoperative day, with the mean value of 98.7 (statistically significant: P, 0.001). On the 3rd postoperative day, the mean temperature value in the control group had returned to 98.6, whereas no significant alteration was noticed on the 10th postoperative day (mean temperature, 98.6_F).

The rise of body temperature in the study group postoperatively was accompanied by some consistent characteristics: The temperature's peak occurred almost always in the evening, returned to close to normal by the morning, and was easily controlled by simple medication (eg, paracetamol tablet). Furthermore, patients were feeling well and had a good appetite despite having a raised temperature.

Discussion

During the last few years, there has been emerging evidence that reamed intramedullary nailing generates a systemic inflammatory reaction of significant severity [3]. Research is attempting to define the etiology and pathogenesis of this systemic reaction and to investigate the possibility of a relationship between reamed intramedullary nailing and

appearance of severe postoperative complications, such as pulmonary dysfunction in specific patients. Several precipitating causes could be responsible for appearance of this systemic significant alteration of the biologic markers and fever that follow both reamed and undreamed intramedullary nailing.

The amount and quality of reaming products (eg, burnt particles) entering the circulation could be proportional to the magnitude of the systemic reaction, with the pulmonary dysfunction being the principle clinical representative, as suggested by Pape *et al.* [5]

However, more recent studies have contradicted these proposals, concluding that a relationship between intramedullary nailing (reamed or unreamed) and systemic pathology cannot be proven [4, 5, 6]. In the present study, it was not possible to correlate the severe inflammatory reaction observed after reamed and unreamed intramedullary nailing with a systemic clinical entity. The precise role of reaming to the pathogenesis of the inflammatory process was not investigated, because it would involve an additional group of patients treated with unreamed intramedullary nailing. This would be contrary to our current belief that reamed intramedullary nailing is the treatment of choice for the management of closed femoral and tibial shaft fractures.

Another cause for the appearance of systemic inflammatory reaction after nailing could be the increase in bone temperature that happens during the reaming process and also undergoing surgery by both the groups. Giannoudis *et al.* [6] found that significant rise of bone temperature occurs when reaming narrow tibia canals, whereas the generated heat was less with wider canals. It should be mentioned that a local temperature rise could trigger a systemic inflammatory response, but it remained unexplained why the heating effect was related only to narrow tibia.

However, in the present study, there was no significant alteration of ESR, CRP, plasma lactate but temperature between the preoperative measurements in both the study and control groups, whereas acute elevation of the ESR, CRP & temperature but not plasma lactate occurred immediately postoperatively in patients in the study and control group. Because patients in both groups underwent operative procedures to long bones of leg, there was no difference between reamed & unreamed groups for ESR, CRP & TEMP. These 3 parameters raised immediate post operatively & increased further and reached peak on POD 3 and reached near pre-operative value on 10th POD for both groups.

But plasma lactate decreased immediate post operatively and reduced further on 3rd POD and reached near pre-operative value on 10th POD for both the groups.

Anemia caused by trauma and surgery, could play a role in the alteration of the biologic markers [7, 8]. However, hematocrit values in patients in both groups did not correlate with the significant alteration of ESR and CRP, PL or the acute rise and duration of high body temperature in both the groups.

Increase of intramedullary pressure, caused by the insertion of the nail and/or the reamers, could be an additional cause for the initiation of the inflammatory process and development of systemic reaction after intramedullary nailing.

However, this systemic reaction also could be influenced by pressure into soft tissues around fracture, a parameter that has not been investigated so far. The contents of medullary canal are pushed, during reaming & nailing, through fracture to an already congested area, secondary to fracture hematoma & soft-tissue edema.

Conclusion

Both Reamed and Unreamed groups causes significant inflammatory reaction that warrants further investigation. Knowledge that biologic markers are altered could help toward better postoperative management and undisturbed commencement of a physiotherapy program, and also toward better assessment and diagnosis of early postoperative complications, such as infection.

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