
SHORT COMMUNICATION

Specific effects of olive oil-based lipid emulsions in critical care. A preliminary report

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ABSTRACT

Objective: To add to the available information on the effects of a predominantly olive oil-containing fat emulsion in patients with acute and critical illness.

Design: Some specific effects of the infusion of a single-dose ClinOleic 20% emulsion were assessed in patients with acute conditions, in the form of a pilot case study.

Patients: The study included 10 patients in various acute conditions (post-traumatic or postoperative state, infection) requiring parenteral nutrition.

Methods: Total plasma cholesterol, triacylglycerols, squalene, lathosterol, glutathione peroxidase and malondialdehyde were determined.

Results: At the end of the ClinOleic infusion cholesterol remained unchanged, triacylglycerols did not significantly increase, squalene increased markedly ($p < 0.007$), lathosterol did not significantly decrease, and glutathione peroxidase and malondialdehyde remained unchanged. The infusion was well tolerated.

Conclusion: The availability of an emulsion characterized by a low phytosterol supply, which enriches the pool of cholesterol precursors (squalene) with no impact on indices of lipid peroxidation, is particularly desirable in critical illness.

KEY WORDS: Fatty acids, ClinOleic emulsion, Squalene, Malondialdehyde, Glutathione peroxidase

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INTRODUCTION

Lipid emulsions are an indispensable component of parenteral nutrition and play an important role in many settings, including long-term nutritional support and nutrition in critical illness. The most widely used fat emulsions have been based on soybean oil, whose principal components are triacylglycerols derived from polyunsaturated fatty acids (PUFAs, mainly omega-6 linoleic acid). The available data suggest that these emulsions may have undesirable effects, for instance impairment of immune function by altering chemotaxis, decreasing the production of

complement components, and altering the formation of cytokines in monocytes and neutrophils (1-5). In addition, fat mediators derived from PUFAs of the omega-6 series such as linoleic acid are the main source of prostaglandin E₂, thromboxane A₂ (TXA₂) and leukotriene B₄, C₄ and E₄. Overproduction of these mediators might adversely affect pathophysiological processes in critical illness by altering the immune response and vascular permeability, and by stimulating thrombocyte aggregation and increasing blood pressure in the pulmonary vascular bed. Moreover, PUFAs are targets for lipoperoxidative processes and the generation of reactive oxygen species (ROS). This has stimulated the development of new fat emulsions which

may be better balanced in terms of fatty acid composition, thereby limiting undesirable effects. One result has been the development of a fat emulsion in which a decreased omega-6 PUFA content is obtained by replacing a large proportion of the soybean oil with olive oil. This has a high content of the monounsaturated fatty acid oleic acid (C18:1 n-9). The emulsion (ClinOleic 20%, Baxter International, Lessines Belgium) contains 80% olive oil and 20% soybean oil (6), with a spectrum of fatty acid composition including 65% monounsaturated, 20% essential (PUFA), and 15% saturated fatty acids.

We conducted this pilot case study to add to the available information on the use of ClinOleic 20% in patients with acute and critical illnesses. We assessed some specific effects of a single-dose infusion (500 mL of 20% emulsion, equivalent to 100 g of fat) in 10 patients.

PATIENTS AND METHODS

The study included 10 patients with acute conditions (surgical and nonsurgical trauma, wound infection, sepsis; Table I) who were requiring parenteral nutrition. SAPS II

TABLE I - PATIENT CHARACTERISTICS

Diagnosis	Gender	Age (years)
Postoperative (gastric resection)	M	72
Wound infection	F	51
Postoperative (colon resection)	F	88
Postoperative (cholecystectomy)	M	75
Peritonitis	M	55
Trauma (car accident)	M	63
Serious polytrauma (motorcycle accident)	M	23
Serious polytrauma (motorcycle accident)	M	24
Wound infection (phlegmon)	F	76
Trauma (car accident)	M	25

TABLE II - MAIN RESULTS. LIPIDS AND REACTIVE OXYGEN SPECIES, MEANS ± STANDARD DEVIATIONS

	TCH	TAG	SQ	LATHO	GPX	MDA
Pre-infusion	2.80 ± 0.75	1.38 ± 0.81	0.86 ± 0.41	2.27 ± 0.97	40.45 ± 8.47	1.38 ± 1.06
Post-infusion (6 h)	2.77 ± 0.80	1.96 ± 0.97	3.75 ± 0.33	2.17 ± 0.85	38.12 ± 9.78	1.36 ± 1.07
24 h after start of infusion	2.17 ± 0.56	0.83 ± 0.25	0.88 ± 0.11	2.17 ± 0.48	35.74 ± 7.88	1.00 ± 0.46
P value (pre-infusion vs post-infusion (6h))	NS	NS	0.007	NS	NS	NS

TCH, total cholesterol, mmol/L; TAG, triacylglycerols, mmol/L; SQ, squalene, μmol/L; LATHO, lathosterol, μmol/L; GPX, glutathione peroxidase, U/g Hb; MDA, malondialdehyde, μmol/L; NS, not significant

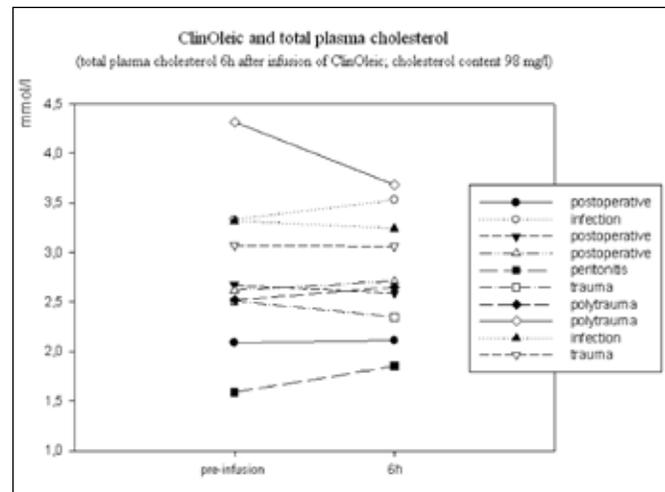


Fig. 1 - Total plasma cholesterol before and at the end of a 6-hour ClinOleic infusion.

scores (7) ranged from 35 to 45. ClinOleic was applied after 4–6 day of hospitalization. Most of the energy intake of the patients was provided by parenteral nutrition, with a minor enteral supply amounting to 500–750 Kcal/day. There was no serious organ failure requiring instrumental support. Venous blood was drawn before the start of the 6-hour ClinOleic infusion, at the end of the infusion, and 18 hours later (24 hours after the infusion had been started). Informed consent was obtained from all patients. Plasma total cholesterol and triacylglycerols were determined by a spectrophotometric method using a modular analyzer (F. Hoffmann-La Roche Ltd, Basel, Switzerland). Glutathione peroxidase and malondialdehyde were determined in erythrocytes and plasma by immunochemical (Randox, Crumlin, United Kingdom) and spectrophotometric methods, respectively. Squalene and lathosterol were determined in plasma samples. These were extracted using the Abell-Kendall method and derivatized to produce

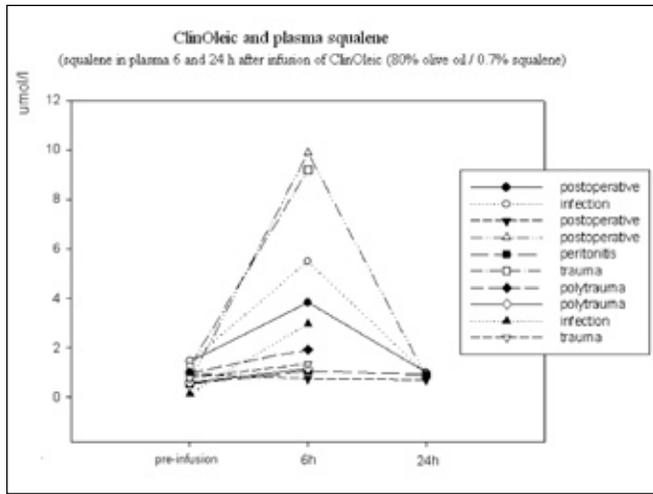


Fig. 2 - Plasma squalene before and at the end of a 6-hour ClinOleic infusion, and 24 hours after the start of the infusion.

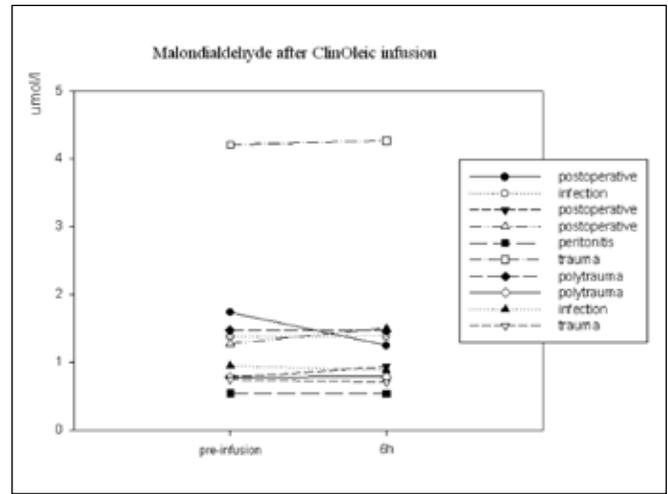


Fig. 3 - Plasma malondialdehyde before and at the end of a 6-hour ClinOleic infusion.

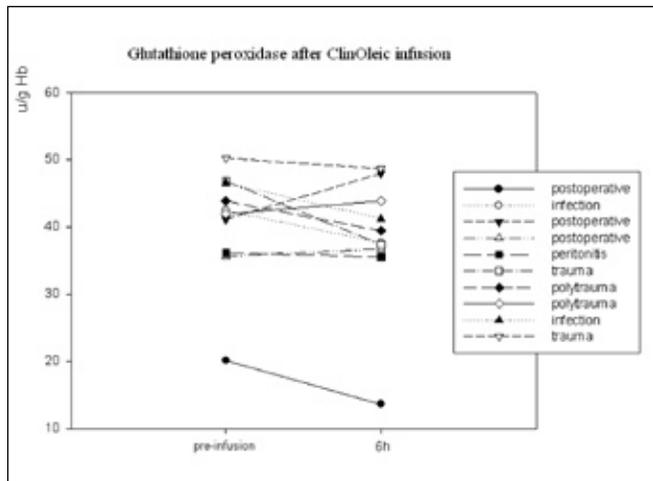


Fig. 4 - Erythrocyte glutathione peroxidase before and at the end of a 6-hour ClinOleic infusion.

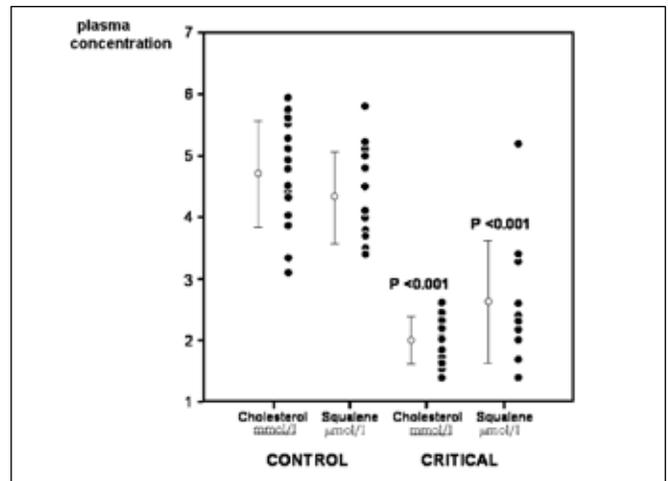


Fig. 5 - Total cholesterol and squalene in critically ill patients versus controls (from reference 11).

trimethylsilyl ethers. The resulting derivatives were analyzed using gas chromatography and detection by mass spectrometry (GC-MS) (Agilent Technologies, Waldbronn, Germany). The obtained results were analyzed using the statistical software SigmaStat (Systat, Chicago, IL, USA). The protocol complied with the Helsinki declaration of 1975 and was approved by the Institutional Review Board.

RESULTS

The mean ± standard deviations of the results are detailed in Table II. After infusion of the fat emulsion, mean plasma cholesterol remained unchanged (Fig. 1) and triacylglycerols increased but not significantly. Squalene, an important precursor of cholesterol and steroid hormone synthesis, showed a marked increase ($p < 0.007$); squalene values were also assessed at 24 hours (Fig. 2). Lathosterol decreased, but not significantly. ClinOleic infusion did not result

TABLE III - BIOLOGICAL EFFECTS OF THE DEFICIENCY OF CHOLESTEROL AND ITS PRECURSORS

Specific deficiency	Potential effects
Cholesterol depletion in tissues	Inadequate synthesis, destruction and dysfunction of cell membranes
Isoprene and farnesol depletion	Deficient isoprenylation signal proteins (mediators)
Ubiquinone deficiency	O ₂ transport disturbances
Dolichol deficiency	Failure of glycoprotein synthesis
Lack of squalene	Impaired immunity, low resistance to stress

in increased values of malondialdehyde or glutathione peroxidase, biological indicators of lipoperoxidation and ROS formation (Figs. 3 and 4). There was excellent tolerance to the infusion.

DISCUSSION

These results on the effects of an olive oil-based fat emulsion elicit several observations. Cholesterol depletion is relatively common in critical illness. This is consistent with the findings of several studies (for instance, references 8, 9 and 10) and the findings and concepts reported in Figure 5 and Table III. The availability of an emulsion which may provide cholesterol or enrich the pool of its precursors such as squalene, with a concomitant low supply of phytosterols, is particularly desirable not only in the setting of chronic malnutrition, but particularly for critically ill patients (8, 11, 12). An additional important aspect is the avoidance of lipid peroxidation and ROS formation (for instance, the formation of relatively dangerous hydroperoxides) with parenteral fat supply, and the data on malondialdehyde and glutathione peroxidase in Figures 3 and 4 after ClinOleic administration are particularly reassuring in this regard. The results reflect advantages connected to the photochemical and thermal stability of the emulsion. These may be cumulatively related to its natural richness in monounsaturated oleic acid (which is less prone to lipoperoxidation) in comparison with PUFAs (which are essential, but more exposed to lipoperoxidation) and its natural richness in vitamin E (13).

The excellent tolerance to the infusion observed in acute conditions, the signs of improved availability of cholesterol and squalene, the absence of any relevant impact on ROS formation, and the particularly low

phytosterol content are important advantages of this emulsion. These findings implement already available information on the main effects of olive oil-based lipid emulsions (5, 14-19) and point to the need for additional, more extensive investigations into the specific aspects assessed in our preliminary case study.

Conflict of interest statement: none.

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