Lymphology 8 (1975) 123-126

Failure of Intestinal Lymphatic Block to Prevent Experimental Hypercholesterolemia

Peter J. Wilk, Ramesh C. Karipineni, Callisto A. Danese

Department of Surgery, Mount Sinai School of Medicine of the City University of New York, New York, U.S.A.

Summary

Intestinal lymphatic blockade was produced in dogs by ligating the individual lymphatics and then obturating them with an acrylic solution. Despite meticulous technique a complete and lasting lymphatic block could not be produced. Extensive collateral channels developed via the omental, the colonic, the renal and the retroperitoneal lymphatics.

Some of the vessels recanalized. Absorptions studied using C-14 octanoic and H-3 oleic acid suggested that although the lymphatic blockade was partially successful in lowering the content of oleic and octanoic acid in the lymph, direct lymphovenous transport compensated for the lymphatics' obstruction. The cholesterol values of the lymph blocked dogs were not lower than those of the controls. Intestinal lymphatic obstructions does not appear to be a practical approach to the prevention or treatment of hypercholesterolemia.

Introduction

Hypercholesterolemia is associated with progressive arteriosclerosis in man (1, 2). Cholesterol and long chain fatty acids are absorbed via intestinal lymphatics (2). This study tests whether their absorption could be prevented by blockade of the intestinal lymphatics.

Materials, Methods and Results

Fifteen adult beagles with an average weight of 10 kg were studied. Eight dogs underwent laparotomy alone and served as controls.

In 7 dogs a surgical intestinal lymphatic block (3) was produced. Prior to operation these animals were fed a half milk-half cream mixture so that the intestinal lymphatics could be clearly seen. The intestinal lymphatics were individually ligated as they entered the thoracic duct and then were ligated again at their confluence with the mesenteric lymph node. All individual intestinal lymph vessels were then cannulated at the intestinal border and were injected with an acrylic solution* that filled their lumen from the intestinal border to the ligated mesenteric lymph node. Lastly, the lymph node was injected directly with the acrylic solution. All lymphatics were blocked from the duodenum to the ileocecal valve. In none of the animals was the integrity of the lumen disturbed. All animals were reexplored twice at intervals of two months.

Prior to these reexplorations the animals were again fed a mild-cream mixture to permit visualization of the unblocked lymphatic channels. At the first reexploration, all animals had dense omental adhesions to the serosa of the thickened bowel. Extensive lymphatic collateralization was evident within the mesentary. Cream flowed freely along the omental lymphatics. Omentectomy and further injection and ligation of all visible lymphatics were performed. Intestinal biopsies were taken. After 2-3 procedures, the bowel was markedly thickened and histological sections of the biopsies confirmed the gross impression of lymphedema. When we were satis-

*The solution was obtained as Batson's anatomical compound from polyscience incorporated of Rydal, New Jersey

fied that as thorough a block as possible had been established the animals were entered into the project in the experimental group.

All 15 dogs were made hypothyroid with oral I^{131} (0.5 mCi/kg)* plus oral thiouracil (1 gm/day). The dogs were fed standard diets with cholesterol supplements (3 gm/day for 2 months and 10 gm/day for 5 months). Vitamins A, D, E, and K were given parenterally at weekly intervals. Serum cholesterol concentrations were measured before surgery and after surgery at monthly intervals.

All animals remained clinically well and maintained their weights. No changes in serum chemistries other than low PBI's were observed. The animals with intestinal lymphatic block had bulky stools but no diarrhea. Mean serum cholesterol measurements in control and lymph blocked dogs were as follows:

Table 1. Serum cholesterol concentration in mg% before and after cholesterol supplemental diet

		Months on diet						
	pre-diet	1	2	3	4	5	6	7
Controls (8 dogs)	171	461	453	525	589	683	513	649
lymph blocked (7 dogs)	199	298	397	702	870	608	780	1064

Serum cholesterol levels in lymphatic blocked dogs were not significantly different than control dogs.

After seven months from the time the animals began the cholesterol supplement diets, the animals were again reexplored and then sacrificed. Prior to surgery the animals were fed a milk-cream mixture. Five of the animals (3 controls, 2 lymph blocked) were also fed a milk-cream mixture that contained 30 μCi C-14 octanoic acid (250 μCi/mMol n-octanoic acid-1-C-14 sodium salt)** and 625 μCi H-3 oleic acid (5 mCi oleic acid 9,10 H-3(N) 2-5 Ci/mMol)**.

At exploration it was evident that most of the blocked lymphatics had remained blocked but that new collaterals had developed. There were tributaries to all adjacent anatomical organs – the colon, the kidneys and the retroperitoneum.

The edema had largely subsided although minimal thickening of the bowel persisted.

In the 5 animals fed labeled fatty acids, simultaneous samples of vena cava blood, portal vein blood and thoracic duct lymph were obtained and counted. The results of these samples were as follows:

Table 2. Absorption of labeled fatty acids in lymph blocked dogs expressed as percentage of controls

Specimen	Lymph		Portal Vein		Vena Cava	
	Oleic	Octanoic	Oleic	Octanoic	Oleic	Octanoic
Average lymph blocked animals (1% of average absorption of controls)	55	75	73	544	115	601

*Squibb laboratories
**obtained from new England Nuclear Corp., Boston, Mass.

Discussion

Hyperlipidemia, especially hypercholesterolemia, is one of the most important pathogenetic factors in the development of arteriosclerosis in man (1, 2). As lipids are absorbed via intestinal lymphatics it is reasonable to expect that intestinal lymphatic obstruction would curtail their absorption. In this experiment, however, we were unable to produce a significant and long-lasting block of the intestinal lymphatics.

Attempts to produce a permanent regional lymphatic block have been made using a variety of techniques (3, 4). The primary difficulty encountered is the fact that lymph, unlike blood, does not clot easily and does not organize. Therefore, simple ligature of intestinal lymphatics, although effective in producing temporary lymphostasis, is inefficient in the long run as the ligature is extruded and the lumen reconstituted.

Removal of a short segment of lymph vessel is also ineffective as the lymph vessels are able to regenerate (5). However, if the excision involves a long segment regeneration fails to reconstitute the removed vessels and lymphatic flow is dependent on the potential for collateral flow.

Obturative obstruction of lymphatic vessels is more efficient, especially if the obturating substance is irritating to the vessel wall and produces adhesions and a permanent bond within the vessel (3).

This approach was followed in our technique and the majority of the intestinal lymphatics remained blocked for the duration of the experiment. In a few instances, however, we observed that the obstructed lymph vessels had dilated and the obstructing substance had fragmented within the lumen. The lymph within these vessels was thus able to flow around the fragmented substance and past the proximal ligature which had cut through the vessel and had been extruded.

While the majority of the vessels remained obstructed, the other compensatory mechanisms slowly developed and markedly decreased the effectiveness of the lymphatic blockade. First, at each reexploration "new" lymph vessels were observed side by side with the obstructed lymphatics. Evidently these were previously minor vessels which then enlarged and assumed a major role in lymph flow. These vessels were blocked at the subsequent reexploration. As the mesenteric blockade became more complete, collateral flow was observed to the retroperitoneal, the renal and colonic lymphatics.

Another possible compensatory mechanism for lymphatic blockade is the development of lymphovenous communications (6, 7). These have been shown to occur in different circumstances following lymphatic obstruction.

The observation that the lymphatic blocked dogs had serum oleic acid concentrations equal to that of the controls while they had decreased oleic acid in the lymph suggests that direct lymphovenous transport occurred. We have no explanation for the observed elevation of octanoic acids in portal and vena cava samples.

The technique described here has been used previously to successfully produce lymphedema of short duration (3). However, in this long duration experiment the compensatory mechanisms described made the lymphatic block neither complete nor long lasting. Although one could hypothesize that a better technique might be more effective, our observations suggest that this would be difficult to achieve. Therefore, we are unable to explain the reported significant falls in serum cholesterol levels observed by *Servelle* (8) and *Monserrat* (9) in their patients after simple ligature of mesenteric lymphatics.

We would conclude that we have been unable to produce in dogs a long-lasting blockade of intestinal lymphatics capable of curtailing the absorption of cholesterol. These results make us skeptical of the practicality of lymph block in the prevention and/or treatment of hypercholesterolemia.

References

1 *Levy, R.I., D.S. Fredrickson, R. Shulman, D.W. Bilheimer, J.L. Breslow, N.J. Stone, S.E. Lux, H.R. Sloan, R.M. Krauss, P.N. Herbert:* Dietary and drug treatment of hyperlipoporoteinemia. Ann.Intern.Med. 77 (1972) 267

2 *Buchwald, H., R.B. Moore, R.L. Varco:* Surgical treatment of hyperlipidemia. Circulation 49, Suppl. I (May 1974)

3 *Danese, C.A., M. Georgalas-Panesis, A.E. Kark, D.A. Dreiling:* Studies of the effects of blockage of intestinal lymphatics. I. Experimental procedure and structural alterations. Am.J.Gastroenterol. 57 (1972) 541

4 *Kalima, T.V.:* The structure and function of lymphatics and the influence of impaired lymph flow on the ileum of rats. Scand.J.Gastroenterol. 6, Suppl. 10 (1971) 1

5 *Danese, C.A., J.M. Howard, R. Bower:* Regeneration of lymphatic vessels. A radiographic study. Ann.Surg. 156 (1962) 61

6 *Neyazaki, T., E.A. Kupice, W.H. Marshall, M.L. Abrams:* Collateral lymphovenous communication after experimental obstruction of the thoracic duct. Radiology 85 (1965) 423

7 *Threefoot, S.A., M.F. Kossover:* Lymphaticovenous communications in man. Arch.Intern.Med. 117 (1966) 213

8 *Servelle, M., F. Fouffilange, J. Andrieux, H. Perrot, J. Soulié:* Ligature des lymphatiques intestinaud et artériosclérose (27 mois d'expérience). Semaine des Hôpitaux des Paris 45 (1969) 571

9 *Monserrat, J., F. Ballesta, L. Torre:* Arteriosclerosis oblitante cuadrimélica. Hipercolesterinemia e hiperlipemia. Ligadura del tronco linfático intestinal. Angiologia 23 (1971) 64

Callisto A. Danese, M.D., 19 East 98th Street, New York, NY 10029, U.S.A.

Lymphology 8 (1975) 126-135

The Effect of Anaesthesia and Surgery on Lymph Flow, Protein and Leucocyte Concentration in Lymph of the Sheep

J.W. Quin, A.D. Shannon

Department of Experimental Pathology, John Curtin School of Medical Research, The Australian National University, Canberra, Australia

Summary

Anaesthesia and the trauma of surgery, associated with the cannulation of lymphatic ducts in various regions of the body of the sheep, had a profound effect on lymph flow, protein concentration and leucocyte concentration of lymph. In general lymph flow was depressed and the protein concentration elevated in lymph collected at the time of cannulation, or within the first 24 hours of recovery from surgery. The changes in protein concentration in lymph draining the peripheral regions of the body appeared to be due to surgical interference in the region of drainage. The greatest changes in lymph flow were observed in lymph draining peripheral regions (skin, tendon, muscular areas) while lymph draining soft tissues in central regions (kidney, liver) was less affected by the anaesthesia and surgical stress.

A neutrophilia was observed in venous blood collected under anaesthesia while the overall numbers of lymphocytes in three sources of efferent lymph were depressed. It is suggested that corticosteroid hormones may play a role in the changes in leucocyte migration observed during anaesthesia and surgical stress. Changes observed in the cellular content of afferent lymph appeared to be due to a low grade inflammation associated with surgical interference in the region of lymphatic drainage.

Introduction

Anaesthesia interrupts physiological functions and may result in biochemical and pathological changes in blood and tissues. The nature and duration of these changes are dependent upon the type of anaesthetic agent employed, together with the length and depth of anaesthesia.