Correspondence
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Continuous administration of prostaglandin E_1 for hyperbilirubinemia after extended right hepatic lobectomy

A high serum level of total bilirubin is a significant risk factor for a poor prognosis after major hepatectomy for liver cancer.[1] However, effective therapy for hyperbilirubinemia has yet to be established. Prostaglandin E_1 (PGE_1) has been reported to increase portal blood flow,[2] improve hepatic function,[3–5] and protect the hepatocytes from various injuries.[6,7] It is expected that PGE_1 may damatically improve metabolic impairement after major hepatectomy. We report a case of hyperbilirubinemia after extended right hepatic lobectomy for metastasis from rectal cancer. The patient was managed effectively with continuous administration of PGE_1.

Case report

A 52-year-old man was admitted because of liver metastasis from cancer of the rectum, which had been resected 1 year before. The only abnormality on laboratory investigation was a serum carcinoembryonic antigen level of 38 ng/mL. Two weeks after admission, an extended right lobectomy was done to remove multiple liver tumours in S4, S5, S6, S7 and S8. Immediately postoperatively, the serum total bilirubin level was extremely high at 152.2 μmol/L (normal 3.4 to 17.1 μmol/L) (direct 23.9 μmol/L, indirect 128.3 μmol/L). Systemic intravenous infusion of PGE_1 (0.015 μg/kg/min^{-1}) was started to improve hepatic function and protect hepatocytes. Continuous administration of PGE_1 for 2 days reduced the serum total bilirubin level to 106.0 μmol/L with a decrease in blood pressure. However, withdrawal of PGE_1 for 1 day resulted in an increase in the bilirubin level to 183.0 μmol/L (direct 61.6 μmol/L, indirect 121.4 μmol/L). Other laboratory findings on the fourth postoperative day indicated that the patient was almost in liver failure (Table I). Continuous infusion of PGE_1 was begun, resulting in gradual normalization of the patient's liver status. After 7 days of continuous PGE_1 administration, the serum total bilirubin level had decreased to 56.4 μmol/L and the platelet count had increased to 100×10^9/L. The PGE_1 infusion was stopped on the 15th postoperative day without any increase in the serum bilirubin levels. Thereafter, the patient's clinical course was uncomplicated.

Discussion

In this case, the continuous infusion of PGE_1 produced a dramatic decrease in the serum level of total bilirubin, without hypotension. This effect can be attributed to 2 mechanisms: increased hepatic blood flow by PGE_1,[2] accelerated bilirubin metabolism in hepatocytes; and increased intracellular levels of cyclic 3′,5′-adenosine monophosphate in hepatocytes by PGE_1[8] stabilized the hepatocellular membrane, protected hepatocytes and maintained hepatic function, including bilirubin metabolism. PGE_1 has been reported to improve impaired hepatic function, including ammonia metabolism,[4] glyconeogenesis[5] and DNA synthesis.[9]

We have reported another action of PGE_1 on impaired hepatic function that indicates that it may be one of the most efficacious substances for critical hepatic disorders after hepatectomy, including hyperbilirubinemia.

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Table I

Laboratory Findings on the Fourth Day After Extended Right Hepatic Lobectomy

Test	Result	Blood measurement	Result
Total serum protein, g/L	53	Leukocyte count, $\times 10^9$/L	10.3
Serum albumin, g/L	37	Red cell count, $\times 10^{12}$/L	226
Blood glucose, mmol/L	23.2	Hemoglobin, g/L	76
Serum urea nitrogen, mmol/L urea	3.5	Platelet count, $\times 10^9$/L	57
Serum creatinine, μmol/L	62	Prothrombin time, % of standard	36.6
Serum bilirubin, μmol/L		Antithrombin III, %	45
Total	183	Hepaplastin test, % of standard	27.23
Direct	62	Osmolality, mOsm/kg	304
Indirect	121		
Serum aspartate aminotransferase, U/L	29		
Serum alanine aminotransferase, U/L	50		
Serum lactate dehydrogenase, U/L	302		
Serum alkaline phosphatase, U/L	181		
Serum cholinesterase, U/L	174		
Serum amylase, U/L	33		
Plasma ammonia (NH_3), μmol/L	67		

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Guideline for managing breast lumps

The editors have stated that they would like to receive and publish comments from readers of the Journal. I would therefore like to comment on the letter concerning a guideline for the management of breast lumps by Mahoney and colleagues (*Can J Surg* 1998;41[6]:476-7).

To issue algorithms or guidelines without the supporting rationale or evidence is not a valid exercise. To understand what is involved in developing guidelines, I would respectfully refer the editors to the methodology of the practice guidelines development cycle.[1] This process is used by the Ontario Cancer Treatment Practice Guidelines Initiative. The purpose of the Initiative is to improve the outcomes for cancer patients, to help practitioners apply the best available research evidence to clinical decisions and to promote responsible use of health care resources. The development of guidelines is clearly a time-consuming iterative process. One might infer, erroneously or not, that a group of interested individuals in the University of Toronto has arrived at a "consensus" over a cup of coffee.

With reference to Mahoney's algorithm on page 477, what is the evidence underpinning the recommendation that a 45-year-old woman with no clinical evidence of breast cancer and no risk factors be subjected to biannual mammography?

The risk of breast cancer increases with age. The Ontario Breast Screening Program provides screening only for women 50 years of age or older. Even for this group of women, the evidence of benefit is sparse, and some would argue that the risk of harm outweighs any putative benefit.

If the editors of the Journal are looking forward to developing a series of credible guidelines for managing common surgical problems, they must stipulate the methodology to be employed. Like it or not, we are living in an era of evidence-based surgery.

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Reference

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Dr. Leo Mahoney and my colleagues at the University of Toronto in their letter in the December issue of the Journal (*Can J Surg* 1998;41[6]:476-7) outlined their recommended procedure for a family doctor to deal with a breast lump.

Their advice about cysts is reasonable. Having treated 8 patients with a cancer that was in the wall of a cyst or adjacent to a cyst, I can verify that all of them were detected by dark or maroon-coloured blood on aspiration of the cyst or by the persistence of a lump after aspiration. The fluid usually aspirated from a cyst does not need to be sent for cytologic examination as they correctly observe.

However, they fail to mention that the cells from a solid lump should definitely be sent for examination. Pathologists are very accurate in confirming the diagnosis on cytologic examination. It is not good practice to stick a needle into a lump and then discard the cells. The cells in the bar-

rel of that needle will supply a diagnosis. Anyone who aspirates a breast lump should obtain slides and pathological confirmation.

Edward B. Fish, MD
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Dr. Mahoney responds

I and my colleagues wish to reassure Dr. Gately that this guideline is consistent with those that already exist.[1] We have adapted it to the perspective of a primary care physician and focused it to manage any medicolegal concerns related to a delayed diagnosis of breast cancer.[2]

Even if there are no clinical findings or the woman's breast cyst disappears on aspiration, our 45-year-old patient should have mammography as part of her complete assessment.[1] If the mammogram is normal, as expected, it automatically becomes the baseline for a regular biannual mammographic screening program. For the purpose of simplicity, we chose to recommend it as such, rather than as part of the diagnostic evaluation. Whether the next mammogram should be obtained in 2 years, as recommended by the National Cancer Institute,[3] or in 5 years, as recommended by most world authorities, including the National Cancer Institute of Canada,[4] is debatable.

Our 45-year-old woman thought she had a palpable lump and was informed and concerned enough to report to her family physician for an examination. Like most Canadian women, she likely obtained her information from media sources originating in the United States, which promote mammographic screening beginning at 40 years of age. In view of her obvious concern about her personal breast health, in our view it was prudent to offer, for her consideration, access to biannual mammography at age 47 years instead of 50 years.

Dr. Fish refers to the fact that most consultant surgeons will aspirate cells from a solid breast lump and send them for cytologic examination. They are well aware of the delays and errors that sometimes occur in the process. At the same time they have the opportunity to arrange for excisional biopsy, which will be necessary to establish an unequivocal diagnosis.

From the standpoint of the family practitioner, however, for whom this guideline was prepared, I and my colleagues believe it is much simpler, easier and safer to refer the patient immediately and directly to a surgeon.

Delay in diagnosis of breast cancer has become a worrisome cause of medicolegal litigation for both surgeons and family practitioners.[2] By immediate referral, as recommended in our guideline, the family physician can avoid any such stressful experience.

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