

Intestinal adaptation to an elemental diet

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Elemental diets, also known as chemically-defined diets or defined-formula diets, are complete liquid nutritional preparations containing a full range of nutrients for the maintenance of normal physiological functions. They contain basic nutritional components (purified L-amino acids alone or with a protein hydrolysate), simple carbohydrates, essential lipids, vitamins, minerals and trace elements. They are presented to the gastrointestinal tract in a readily-assimilable form, being almost completely absorbed in the upper gastrointestinal tract without the requirement of full digestive processes (Russell, 1975, 1981).

The principal elemental diets are Vivonex and Vivonex HN (Eaton), Flexical (Mead-Johnson), Nutranel (Roussel), Precision preparations LR and HN (Doyle), at present not available in the UK, and Elemental 028 (Scientific Hospital Supplies).

Elemental diets were the first complete oral nutritional preparations. In recent years, new polymeric preparations have been developed, complete nutritional preparations which contain undigested proteins as the nitrogen source and a mixture of starch hydrolysates and long-chain triglycerides as the energy source. These preparations require normal or near-normal digestive and absorptive functions in the gastrointestinal tract. A range of preparations of this type is now available, including Clinifed preparations (Iso, 400, Favour, Protein-Rich; Roussel), Ensure (Abbott-Ross), Isocal (Mead-Johnson), Triosorbon (Merck), Express preparations (Introductory, Standard, High Energy) (Express Nutrition), Enteral 400 (Scientific Hospital Supplies), Fortison preparations (Standard, Energy Plus, Soya, Low Sodium) (Cow and Gate), Nutrauxil (Kabi Vitrum).

Nutritional support can also be provided by nutritional supplements which are not complete nutritional preparations by themselves.

The aims of the present paper are to consider the properties of elemental diets and their effect on gastrointestinal structure and function, and from that to assess how best they can be used clinically.

Properties of elemental diets

The intrinsic properties of elemental diets and polymeric diets are listed in Table 1.

Nutritional efficacy. The original experimental formulas were shown to maintain normal nutritional indices in normal subjects (Winitz *et al.* 1970). Recent studies have confirmed this (Yeung *et al.* 1979; Jones *et al.* 1983) but it should be

Table 1. *Properties of elemental diets and polymeric diets*

	Elemental diets	Polymeric diets
Nutritional efficacy	Good	Good
Digestion requirement	Minimal	Normal digestion required
Absorption	Almost completely absorbed in upper gastrointestinal tract	Normal absorptive function required
Residue	Minimal	Low
Hypoallergenicity	Yes	No
Palatability	Poor	Good

noted that the ability of any preparation to correct catabolic conditions in various disease states depends on the severity of nutritional deficiency present and the ability of the patient to ingest adequate amounts of the preparation. Elemental preparations do not appear to be superior to polymeric diets in improving nutritional efficacy in patients with normal gastrointestinal function; more information is required in patients with abnormal gastrointestinal function.

The source of non-essential amino acid-N may be important. In Vivonex HN, most of this is in the form of glutamine and glycine and, in a recent study, retention of absorbed N was less with Vivonex HN than with solid food and a predigested protein diet, and an increase of urea-N occurred with Vivonex HN (Smith *et al.* 1982).

Digestion and absorption. Nutrients from elemental diets are considered to be efficiently absorbed in the upper gastrointestinal tract without the requirements of full digestive processes. Early studies demonstrated that this was so in normal subjects, and the absorption of nutrients from Vivonex has been shown to be comparable to that from a crushed-food homogenate in normal healthy subjects, using a small intestinal perfusion system (Hecketsweiler *et al.* 1979).

Residue. Elemental diets are of minimal residue. A recent study has compared the effects of elemental and polymeric diets on faecal residue in rats (Main *et al.* 1984). Faecal residue (daily dry weight) was measured during the last 14 d of each 28 d feeding period. The diets tested included Vivonex, Vivonex HN, Flexical, Ensure, Clinifed Iso and control rat diet. All test diets had a faecal residue of <8% of the high-residue control diet but Vivonex and Vivonex HN had a lower faecal residue (230 (SE 9) and 180 (SE 20) mg/d respectively) than Flexical (420 (SE 30), $P < 0.01$), Ensure (390 (SE 30), $P < 0.01$) and Clinifed Iso (570 (SE 50), $P < 0.01$).

Effect of elemental diets on gastrointestinal structure and function

The effect of elemental diets on the metabolic and physiological functions of the gastrointestinal tract is important in determining how the gastrointestinal tract

alters or adapts to the use of these preparations. A study of these effects should provide guidance towards the rational clinical use of elemental diets.

Bacterial flora of the gastrointestinal tract. Elemental diets do not have a profound effect on the various types of bacteria present in the alimentary tract, but reduce the overall bacterial mass present in intestinal contents (Hudson *et al.* 1981). The metabolites of the microflora are reduced during elemental diet therapy.

Gastric emptying and secretion. Gastric emptying has been shown to be delayed 30–60 min by both Vivonex and Flexical when given by bolus feeding through a nasogastric tube, compared with blenderized food of similar nutritional content (Bury & Jambunathan, 1974). Some reduction of gastric acid secretion may also occur. Neither of these findings are of practical clinical value in the use of these preparations.

Small intestinal structure and function. Studies on the small intestine in rats have shown that both Flexical and Vivonex significantly increase villous height and decrease the ratio, crypt height:villous height in both jejunum and ileum, suggesting a possible reduction of cell turnover (Nelson *et al.* 1978); few significant changes in intestinal function were observed, as assessed by enzyme activity and intestinal absorption measured by a perfusion system.

Morin *et al.* (1980) compared the effect of isoenergetic amounts of Vivonex, oral solid food and an equivalent diet given intravenously, on intestinal mass and found that it was well maintained by Vivonex in the proximal small intestine, but less well than solid food provided orally. The distal small intestine and colon in rats given Vivonex atrophied and became similar to those on intravenous feeding within the time-course of the study.

Fenyo & Hallberg (1976) studied the effect of an elemental diet (Vivonex) on the intestinal mucosa after jejunum-ileal bypass in the rat and found that after 2 weeks hypertrophy of the functioning part of the small intestine occurred together with atrophy of the blind loop.

These observations confirm that an elemental diet is as effective as a normal diet in inducing intestinal adaptive changes, and provide a basis for the possible use of these preparations in the management of the short-bowel syndrome in man.

Exocrine pancreatic function. Elemental diets require minimal digestion and thus absorption can occur in the absence of normal pancreatic exocrine secretion. There have been conflicting results on the effect of the preparations on pancreatic exocrine secretion. Traverso *et al.* (1981) compared Vivonex HN with intravenous feeding on pancreatic proteolytic activity and ultrastructure, and found that the synthesis and release of proteolytic enzymes was reduced by the elemental diet and that this reduction was equivalent to that which occurs with intravenous feeding. Vidon *et al.* (1978) infused Vivonex and isoenergetic crushed-food homogenate into the normal human jejunum and measured lipase (*EC* 3.1.1.3) and chymotrypsin (*EC* 3.4.21.1); they found that the homogenate caused greater pancreatic enzyme secretion than Vivonex and this secretion increased in relation to its energy and N contents.

These results suggest a basis for the use of elemental diets in chronic pancreatic insufficiency and cystic fibrosis, when adequate absorption of nutrients can be achieved in the absence of full digestive function. They may also be of value in healing pancreatic fistulas because of the reduced exocrine pancreatic stimulation.

Bile acid metabolism. The effect of Vivonex and Flexical on faecal bile acid excretion and cholic acid half-life in rats has been studied (Nelson, 1979). Total faecal bile acids were significantly reduced by both preparations and cholic acid half-life increased, without altering the bile acid pool (Table 2). The changes were more marked with Vivonex than with Flexical but did not differ significantly with the different compositions of these preparations. This suggests that the low fat content is not the most important property in this respect but that low fibre may be a more important influence. It was also found that both elemental diets increased total liver lipid from 5.9 (3.6–7.3) to 8.3 (7.2–12.6) mmol/kg for Flexical and 25.7 (14.1–29.8) mmol/kg for Vivonex ($P < 0.005$). Hepatic histology showed marked fatty change in Vivonex-fed animals and slight changes in those given Flexical.

These findings suggest a basis for the use of elemental diets, especially Vivonex, in conditions where faecal excretion of bile acids needs to be reduced. However, the composition of Flexical may be preferable if the development of fatty liver during long-term elemental diet therapy is to be avoided.

Hypoallergenic and immunological effects. Elemental diets, and particularly Vivonex, have been considered to be hypoallergenic; Vivonex was not immunogenic in rabbits using the precipitin reaction for passive cutaneous anaphylactic response (Galant *et al.* 1977) and the immune status of mice reared on Vivonex was reduced compared with that of mice reared on normal food (Ferguson *et al.* 1978, 1980). In these animals, cell-mediated immunity was

Table 2. *Effect of the elemental diets Vivonex and Flexical on faecal bile acid excretion, cholic acid half-life and bile acid pool size in rats (Nelson, 1979).*

	(Mean values with their standard errors)							
	Control diet		Vivonex		Control diet		Flexical	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Total faecal bile acids at week 7 (mg/kg body-wt per week)	366.1	20.4	77.5	11.7	329.0	51.8	54.3	12.3
		$P < 0.002$				$P < 0.01$		
Cholic acid half-life (d)	2.32	0.23	9.92	0.85	1.57	0.09	6.43	0.55
		$P < 0.002$				$P < 0.01$		
Estimated bile acid pool size (mg/kg body-wt)	165.3	28.1	145.3	22.2	56.7	5.7	76.3	10.5
		NS				NS		

NS, not significant.

normal, but there was an impaired capacity to make antibodies and impaired antiparasite immunity.

These results suggest a possible basis for the use of elemental diets in allergic and immunological conditions such as food allergy, and possibly Crohn's disease.

Clinical uses of elemental diets

On the basis of the data available on the properties and adaptive changes in the gastrointestinal tract of elemental diets, a rational assessment of their clinical uses can be made.

Nutritional support. Elemental diets are no better than polymeric diets in improving and maintaining nutritional status in normal people and probably also in patients with disease processes. They are less palatable and more costly, and probably have little part to play in purely increasing or maintaining nutritional support.

Provision of bowel rest. Elemental and polymeric preparations are all of low residue, although Vivonex and Vivonex HN have very low or minimal residue. When it is considered that fistula healing is dependent on improvement of nutritional status as well as the provision of bowel rest, polymeric preparations are probably as good as elemental diets in this respect, with the probable exception of pancreatic fistulas.

Short-bowel syndrome. The provision of nutritional support with rapid absorption in a short area of small intestine and promotion of intestinal adaptation, make elemental diets of possible value in the management of the short-bowel syndrome. This has been demonstrated in patients with the short-bowel syndrome given Flexical (Voitk *et al.* 1973), and in providing nutritional support and promoting adaptation in children with the short-bowel syndrome (Christie & Ament, 1975).

Chronic pancreatic insufficiency and pancreatic fistulas. The minimal digestion requirement and reduction of pancreatic exocrine stimulation make elemental diets of theoretical value in chronic pancreatic insufficiency, cystic fibrosis and in the healing of pancreatic fistulas. Pincus *et al.* (1971) improved the nutritional status of seven of eight patients with chronic pancreatitis; and ten of forty-three (36%) children with cystic fibrosis improved nutritionally with Flexical over 1 year, the principal problem being one of palatability (Yassa *et al.* 1978). The successful management of pancreatic fistulas with elemental diets has also been reported (Voitk *et al.* 1973; Bury *et al.* 1971).

Bile-acid-induced diarrhoea and ileal fistula healing. The reduction of bile acid excretion with elemental diets has indicated that these preparations may be of value in the management of bile-acid-induced diarrhoea in patients who are unresponsive to cholestyramine. Nelson *et al.* (1977) found that the mean faecal bile acid excretion was reduced from 6.03 (SE 1.48) mmol/24 h to 2.14 (SE 1.23) mmol/24 h, $P < 0.05$ in six patients during Vivonex treatment; faecal weight was significantly reduced and all patients noted improvement in the diarrhoea with less watery stools and reduced urgency.

Ileal fistula drainage changes have also been reported by the use of an elemental diet (Hill *et al.*, 1975). In patients given Vivonex, fistula fluid output was significantly reduced together with a reduction in sodium, total bile acids and trypsin concentration. The corrosive nature of the discharge was reduced and healing encouraged.

Food allergy and sensitivity. The use of the hypoallergenicity property of elemental diets may be of some value in the diagnosis and management of food allergies and sensitivities. Hughes (1978) studied twenty-seven patients with probable food allergy, who were given Vivonex for 1 week, and found that 70% of these symptoms were relieved. In these patients, Vivonex was continued and selected foods challenged orally, safe diets being established within 3 weeks, and remission occurring in 85% of cases. Dockhorn & Smith (1981) demonstrated that Vivonex for 1 week reduced symptom scores in patients suspected of food allergy. Conditions which may be associated with food allergy may also be improved by the use of Vivonex; these include asthma (Hoj *et al.* 1981), eczema (Hill & Lynch, 1982) and dermatitis herpetiformis (van der Meer *et al.* 1981).

Elemental diets and Crohn's disease. Elemental diets may have some value in patients with Crohn's disease. They can cause nutritional improvement, provide bowel rest, reduce bile acid excretion, and the hypoallergenicity and possible bacteriological effects may also be of value.

They have been used in some patients with Crohn's disease as primary therapy and in one study twenty-nine of thirty-two acute exacerbations settled with the use of Vivonex over 4 weeks (O'Morain *et al.* 1980). A reduction of gastrointestinal protein loss from 190 to 99.5 ml/24 h ($P < 0.05$) with a rise of blood lymphocytes on Vivonex for 4–7 weeks was reported by Logan *et al.* (1981), and improvement in clinical, nutritional and immunological features was found in all ten patients treated with Vivonex for 3 weeks (Morin *et al.* 1982).

Elemental diets may not be better than polymeric diets in providing nutritional support in Crohn's disease and their primary effect on disease activity is still to be proven in well-controlled, prospective studies. They are, however, of value in the treatment of local complications (Russell & Hall, 1979). These include anal and perianal lesions, the management and healing of fistulas, especially pancreatic fistulas, ileostomy complications, and the treatment of bile-acid-induced diarrhoea.

Conclusions

The properties and adaptive effects of elemental diets on gastrointestinal structure and function are described and their clinical uses based on these effects considered.

They are of clinical value in a number of disease states. These are the short-bowel syndrome, chronic pancreatic insufficiency and pancreatic fistulas, bile-acid-induced diarrhoea and ileal fistulas, the diagnosis and management of food allergy and sensitivity, and they may possibly be of value in Crohn's disease.

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