

Acacia gum in chronic renal failure



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The child with chronic renal insufficiency will require renal-replacement therapy (RRT) as renal function progressively declines to a glomerular filtration rate (GFR) of less than 10–15 ml/min/1.73 m². Ideal therapy is a renal allograft from either a living, related or cadaveric donor. Alternate therapies include chronic hemodialysis and peritoneal dialysis [1]; however these therapeutic options are not readily available or economically feasible in countries whose economic systems are still developing. Until such time that a more robust economy has developed that can sustain the cost of these advanced techniques, alternate strategies of RRT should be sought. This issue of *Therapy* includes a special focus supplement by AJ Al-Mosawi on the use of acacia gum (AG) in the management of nitrogenous waste products in uremic children [2].

As noted by Al-Mosawi, protein restriction has been suggested in patients with chronic renal insufficiency since the 1930s [2]. Several groups examined this in a systematic fashion. Both Giordano and Giovatnetti and their groups advocated a low-protein diet (LPD, 2–4 g total nitrogen daily) of high biological value, either in the form of essential amino acids or egg whites [3,4]. These patients showed reduced protein catabolism. Both Walser and Rampton's groups suggested that the ketoacids of amino acids could be employed which would serve as a trap for nitrogen released by catabolism [5,6]. The patients' own transaminases would convert these ketoacids to amino acids, taking up the NH₃ released in metabolism. In the present paper, Al-Mosawi suggests that AG could be used to reduce the burden of nitrogenous waste products [2]. Several issues are pertinent: What is AG? How might AG function? What are the pros and cons of AG? What further information is required?

AG, or gum arabic, is the dried exudate produced by various species of *Acacia*, small, woody, sometimes shrub-like trees native to Africa, in response to wounds in the bark of the tree. Gum yields are highest when the trees are least healthy (e.g., stressed by hot weather, poor soil and lack of water). The uses of AG are many and varied, and date back almost 5000 years to the time of the ancient Egyptians, when it was used as a binder in cosmetics, a component of hieroglyphic ink and in the mummification process.

Most commercial AG is from *A. senegal* or *A. seyal*, and more than 70% of the world's supply is produced and exported by the Sudan. This was brought to the public's awareness in 2001, when a rumor arose that Osama bin Laden owned a significant portion of the AG production in the Sudan and that therefore products containing it should be boycotted. This legend was put to rest by the US State Department, who issued a release stating that Osama bin Laden had been divested of his holdings when he was expelled from the country in 1996. Other major sources include Chad and Nigeria [7].

AG is a colorless and tasteless carbohydrate polymer. Importantly, and unlike most other gums, it is soluble in its own weight of hot or cold water. It is a complex and variable mixture of arabinogalactan oligosaccharides, polysaccharides, glycoproteins and metal salts, and varies in color from white to red [8]. It is used to make paints, inks, adhesives and confections (such as gum drops and marshmallows). It is also used in the textile industry, as an important ingredient in shoe polish, and is used medically as a soothing emollient. Its low viscosity allows it to be used to boost the fiber content of foods or beverages without significantly altering the final texture.

There are several possible reasons why AG could work to reduce nitrogenous waste products in a patient with chronic renal insufficiency. The first hypothesis is that AG acts in the gut to limit protein absorption. In a trial involving 16 patients with a LPD, a supplement of AG at 50 g/day or a placebo (pectin: 1 g/day) was employed [9]. Serum urea nitrogen was significantly reduced during AG versus pectin supplementation. Other gums (xanthan gum, the

product of certain bacteria) can reduce the elevation of uric acid and urea in young (3-week-old) rats fed 0.4% adenine [10]. Moreover, the urinary levels of urea, uric acid and creatinine were reduced after dietary fiber. It is noteworthy that AG does not prevent absorption of water and electrolytes [11,12]. In animal studies, AG can remove nitric oxide (NO) by creating an outward NO gradient [11], and also may enhance water, electrolyte, and sugar absorption, most likely by a paracellular route [12].

A second hypothesis involves immobilization of gut bacteria in AG [13,14]. Dietary fiber may stimulate colonic bacterial proliferation and incorporate gut nitrogenous compounds [13]. Urea permeates the apical surface of the intestine and enters the lumen, where it is hydrolyzed by gut bacteria and ammonia ions are taken up by fiber [14]. Consumption of dietary fiber by fecal bacteria will increase energy available to these bacteria and stimulate bacterial growth. This, in turn, will reduce serum urea or ammonia levels by creating a fecal route of excretion of nitrogen. Hence, any urea or ammonia absorbed into the AG will be further metabolized. Rats fed a fiber-supplemented food mixture had augmented removal of urea by the colon [15]. Rampton and colleagues demonstrated that the fall in plasma urea caused by dietary fiber was probably related to inhibition of bacterial ammonia production in the colon [6].

A third, gut-related hypothesis involving the recycling of urea is the notion is that not only does bacterial protein metabolism of nitrogenous waste occur, but that urea breakdown could provide ammonium ions for transamination and protein synthesis. Various labeling methods have produced conflicting results and this theory has largely been abandoned.

Other explanations for the effect of dietary fibers, in general, and specifically AG, involve their effect on renal function. Oral AG has been shown to have renoprotective properties against gentamicin-induced nephrotoxicity in rats [16,17]. Al-Majed and colleagues hypothesize that AG may protect renal function in part through inhibition of the production of oxygen free radicals that lead to lipid peroxidation [16]. When AG plus gentamicin is compared with gentamicin alone (80 mg/kg/day for 6 days) or to gentamicin and 5% cellulose, gentamicin-induced proximal tubular necrosis, as well as plasma creatinine and urea concentrations, were significantly less severe (histology) and lower (biochemical indices) in the presence of AG than cellulose [16]. Another group

was not able to demonstrate an antioxidant effect of AG when given by mouth at several concentrations to rats [17]. However, it may be protective against free radicals if gentamicin is also administered [16]. This renal protective role of AG has not been tested in humans or in states of chronic renal failure (CRF).

The next obvious question is whether AG has a future as an agent that can serve as an alternative to RRT in children with CRF [19]. The reasons for this potential role in children in developing countries are relatively straightforward. Many children live in countries whose economy cannot afford universal dialytic or transplantation therapy. More than a billion children live in Asia [20], and of these, it is roughly predicted that 10,000–12,000/year will develop CRF. Hence, the need for RRT is great. AG is cheap, presumably safe (as it has been consumed by humans for over 5000 years) and is readily mixed with food, being water soluble. The evidence cited earlier suggests that AG will remove even greater amounts of nitrogenous wastes if used in association with a LPD, as advised by Al-Mosawi [2,17].

Before any recommendation can be made regarding the value of AG, several requirements exist. First, a larger number of patients must be examined, possibly in a prospective, double-blind, placebo-controlled trial. For the placebo arm, patients could be given 5–10% cellulose by weight. A statistical power analysis should be carried out to determine how many subjects would be required to be able to detect significant differences between groups. A statistically significant study would be a necessity in order to recommend the use of AG. A concern in some studies is that plasma urea and creatinine may fall, but that negative nitrogen balance might not be reversed. If this were the case, it would pose another shortcoming.

Even if AG were shown to improve the removal of nitrogenous waste products, this therapy would forestall the need for dialysis only in the short term. Long-term use of AG would, of course, be far better to use in patients with stable renal function than those with rapidly progressive renal disease. For instance, in a child with reflux nephropathy, where renal progression is slow, AG might be of greater use than in a patient with focal segmental glomerulosclerosis or crescentic glomerulonephritis. As stated previously, we do not have sufficient information to recommend AG as a temporizing form of RRT.

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