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Beneficial Effects of Parenteral /Enteral Supplementation of Ala – Glndipeptide (AGD) in Patients with Acute Pancreatitis

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ABSTRACT

Background: *Glutamine (Gln), an abundant amino acid readily synthesised in the body, tends to get depleted in nutritional deficiencies associated with critical illnesses e.g., severe acute pancreatitis (SAP).Low plasma Gln is an independent predictive factor for poor outcome in critical illnesses and Gln administration to patients of critical gastrointestinal diseases is reported to be beneficial. In this study, we evaluated and compared the beneficial effects of parenteral versus enteral Ala– Gln dipeptide (AGD) administration in SAP patients.*

Experimental: *Moderately SAP (MSAP) / SAP patients undergoing treatment at the Asian Institute of Gastroenterology, Hyderabad, were divided in to two groups (n=10 each) and given standard therapy alone (group 1)or along with parenteral AGD (group 2). Effects of treatment were determined on haematological, plasma and vital parameters including abdominal girth; liver, kidney and pancreatic functions; IV fluid infused and urinary volume output; disease severity scores and duration of hospital stay including that in ICU. These were determined and compared between the groups on day 1 and 7 of therapy and within the group between day 7 and 1 of therapy. Differences between day 7 and 1 of each parameter were compared between parenteral and enteral (retrospective data) AGD groups to assess the better route for AGD administration. Data was analysed using Student's "t" test or Mann Whitney U test or one way ANOVA as appropriate.*

Results: *Many parameters were comparable between the two groups on day 1 of therapy. Although on day 7, BUN, serum creatinine, SOFA and Marshall score were higher in parenteral AGD than control group, in comparison with those on day one, parenteral AGD showed significant change in body temperature and Glasgow COMA score only on day 7, while standard treatment affected Hb, HCT, plasma globulin, BUN and SOFA score. Althoughcomparison of values on day 7 of treatment showed no significant differences between enteral and parenteral AGD patients, effects in enteral group were of greater magnitude and in right direction than those in parenteral group. Further, comparison of a parameter within the group, on day 7 versus 1 of treatment, indicated that enteral AGD was better than control and perhaps better than parenteral. Finally, testing differences in the value of a parameter (day 7-1) in enteral and parenteral groups, showed no significant differences between them in disease severity scores, although some parameters (liver function tests and vitals) showed significant differences. Nevertheless, the magnitude of change and its direction appeared to suggest enteral AGD to be better than parenteral. It was intriguing that neither enteral nor parenteral AGD had significant effect on total duration of hospital stay in general, or that in ICU in particular.*

Conclusion: *We conclude that early enteral (naso jejunal) rather than parenteral AGD administration may be associated with better benefits in SAP patients albeit both did not affect total duration of ICU or hospital stay.*

Keywords: *Acute Pancreatitis, Alanyl glutamine dipeptide, parenteral administration, enteral administration, disease severity scores, hospital stay.*

INTRODUCTION

Acute pancreatitis (AP), is a potentially serious illness characterized by an acute necro-inflammatory condition of pancreas [1], with variable involvement of peri-pancreatic tissues and/ or remote organ systems [2, 3]. It is the number one gastrointestinal diagnosis prompting inpatient admission and ranks 21st

amongst all diagnoses requiring hospitalization [4], alcohol and gallstones being its most common causes [5]. Medications, infectious agents and metabolic causes such as hyper-calcemia and hyper-parathyroidism are uncommon causes [6]. Smoking is a modifier in the development of alcoholic pancreatitis [7]. Abdominal pain is the most common symptom which is common in about 95% of cases [8]. Elevated serum amylase and lipase activities are the signature laboratory parameters for the diagnosis of AP [9]. Severity of AP is defined by Atlanta classification which is based on the presence of organ failure and/or local complications and/or at least three of Ranson's criteria, and / or at least eight of APACHE II criteria [10].

Moderately Severe Acute Pancreatitis (MSAP) is defined according to ATLANTA classification, as the presence of transient organ failure or local / systemic complications in absence of organ failure [9]. According to Atlanta Classification, Severe acute pancreatitis (SAP) is defined as the presence of persistent organ failure, which leads to Systemic Inflammatory Response Syndrome (SIRS) [9].

Management of AP is based on disease severity and associated complications. Treatment is primarily conservative, includes bowel rest and intravenous fluid replacement [10].AP, a state of hyper catabolism shows a negative nitrogen balance and is associated with poor clinical outcomes [11]. Early nutrition should be started with a therapeutic intent and nutritional support aims mainly to reduce the disease burden and help maintain positive nitrogen balance. Oral feeding can be initiated in mild AP patients, within 24–72 hours of the disease onset. A recent study showed that initiating re-feeding with low fat, soft diet was safe and could reduce hospitalization, unlike the clear liquid diet [12].

Glutamine (Gln), the most abundant amino acid in circulation and intracellular amino acid pools, is synthesized in skeleton, muscle, brain and lungs. It is a conditionally essential amino acid" due to its increased demand in catabolic states [13]. Gln helps inter-organ nitrogen transport [14], is a fuel for enterocytes, reduces bacterial translocation across gut wall and thus reduces the risk of sepsis [15]. Gln is poorly soluble and highly unstable at room temperature as it readily gets hydrolysed to glutamic acid in aqueous solution. It needs a central venous administration which is very difficult. To overcome this difficulty, the Gln containing dipeptides e.g., L-Ala-L-Gln(AGD),in which Gln is highly soluble and very stable have been used for infusion [16]. Indeed, the commercially available supplement for parenteral use contains the dipeptide: L-Ala -L-Gln (AGD) [17], which is more stable than Gln under acidic conditions and at high temperatures [18].

Elevated Gln uptake is a primary characteristic of all rapidly dividing cells [19]. Indeed during hyper catabolic stress, demand for Gln increases, in response to which skeletal muscle increases Gln secretion leading to loss of muscle mass, an important feature in critically ill patients. In fact reduced plasma Gln levels are associated with higher mortality, increased length of hospital stay and infection [20]. Gln supplementation is reported to reduce the length of hospital stay, decrease gut permeability and plasma endotoxin levels [21]. Interestingly, enteral nutrition by jejunal route is feasible, safe, more practical and easier approach than parenteral nutrition [22]. Indeed some studies in AP patients suggested that regardless of its route of administration, Gln showed greater beneficial effects compared to controls not given Gln [23, 24].

However till date, few studies have compared the beneficial effects of enteral and parenteral AGD administration in AP patients. Limited literature appears to suggest equal or better benefits in AP patients given enteral than parenteral AGD, *albeit* the demonstration of benefits of AGD administration to AP patients is equivocal at best. Also, there have been no serious comparisons of benefits of enteral versus parenteral AGD. Considering the ease and feasibility of enteral than parenteral Gln administration and reported benefits of such supplementation, we compared the beneficial effects of parenteral and enteral AGD administration to SAP patients, in an attempt to determine which route is better for the purpose.

Hypothesis Parenteral administration of Ala-Gln (AGD) to SAP and MSAP patients is as beneficial as the enteral route of administration.

MATERIALS AND METHODS

The study was performed at Asian Institute Of Gastroenterology, Somajiguda, Hyderabad, India, a tertiary care referral centre for hepato-biliary, pancreatic disorders. This is a retro-prospective observational study. We analysed

data collected prospectively from a few AP patients treated at AIG Hyderabad, with standard (control) therapy without / with parenteral AGD administration, during September 2018 to March 2019. We compared this with the clinical datacollected in an earlier prospective study at AIG, Hyderabad (2012 – 2017), in which AP patients were given standard therapy without / with enteral administration of AGD. The prospective part of the present study was carried out over a 6 month period i.e. from September 2018 to march 2019 at the AIG, Somajiguda, Hyderabad. On the other hand, relevant data collected from the medical records of AP patients treated earlier (2012-17) at AIG [standard therapy alone (n=22) or along with enteral AGD (n=18)], was used for comparison with the prospective data on the effects of parenteral AGD[10].

Moderately Severe Acute Pancreatitis (MSAP) and Severe Acute Pancreatitis (SAP) patients admitted for treatment at the AIG were recruited for this study based on the following inclusion and exclusion criteria:

Inclusion Criteria

Patients with MSAP & SAP ; Age : 18 - 60 years ; Acute physiological and chronic health evaluation (APACHE) II SCORE $\geq$ 8 ; Raised serum pancreatic enzymes (> 3 fold) on admission ; Marshall score : $\geq$ 2 ; Sequential Organ Failure Assessment (SOFA) score $\geq$ 2 ;Persistent Systemic Inflammatory Response Syndrome score (SIRS) $\geq$2 over 48 hrs (Patients positive for any two of the above scores / parameters were considered for inclusion in the present study)

Exclusion Criteria

Chronic pancreatitis ; Renal failure ; End stage liver disease ; Pancreatic cancer ; Pregnant women ; Corticosteroid therapy ; Any form of artificial feeding from the commencement of AP symptoms

Sample Size

Based on the available literature [25], the power of the study was set at 80% with a confidence interval of 95 %. The sample size was calculated to be 18 i.e. 9 in each group using Med CalC software. 146 patients of SAP and MSAP were screened and twenty of them (as per sample size calculated) meeting the set exclusion and inclusion criteria, were admitted in the study. Relevant clinical data from forty patients studied earlier at AIG, Hyderabad was collected from hospital records, analysed retrospectively and compared with the prospective data from 10 AP patients treated recently with parenteral AGD along with standard therapy.

Patient Treatment

Twenty patients admitted for the prospective study were divided in to two groups of 10 subjects each and the following parameters were determined on day 1, i.e., before the starting of the treatment. Patients in both the groups received the standard therapy (iso-caloric:30-35kcal / kg BW / day) and (iso-nitrogenous: 1.5-2g N /kg BW per day).While ten patients received standard therapy alone for seven days (control , group 1, n = 10) , the remaining ten patients were given parenteral administration of AGD (20g of AGD dissolved in 100 ml of normal saline, administered parenterally over a period of 24 hours) in addition to the standard therapy, for a total duration of seven days (group2: Parenteral; n=10).

Parameters determined : Following parameters were determined in AP patients on day 1 to ensure that patients in both groups were comparable before staring the treatment; and on day 7 of treatment, to assess the beneficial effects if any of, parenteral AGD administration as compared to that with standard therapy alone.

1. Total Length of hospital stay and duration of stay in the ICU
2. Parameters on day 1 and day 7 of treatment
    a. Liver and kidney function parameters
    b. Ultra sound and CT scan (for pancreatic necrosis and peri-pancreatic ascitic fluid accumulation)
    c. Vital parameters (body temperature, Systolic and diastolic Blood pressure, pulse rate, respiratory rate)
    d. Haematological parameters (haemoglobin, haematocrit, MCH, MCHC)
    e. Plasma parameters (total protein, albumin and globulin)
    f. Abdominal girth
    g. Disease severity scores (APACHE II, Marshall, SOFA, SIRS)

Statistical Analysis

Data was analysed statistically using SPSS software. Student's't' test or Paired't' test or One way ANOVA were used for the analyses of continuous variables as appropriate. Non-parametric Mann– Whitney U test and Kruskal – Wallis test were used appropriately whenever

the data were not normally distributed or the variation was large. A 'p' value of less than 0.05 was considered statistically significant.

Table1. *Disease severity scores in MSAP and SAP patients given control treatment alone or with parenteral Ala - Gln, on day 1 and day 7of administration*

S No	Parameter	Control Day1	Parenteral Day1	P value	Control Day7	Parenteral Day7	P value
1	Glasgow COMA**(15)**	14.900 ±.3162 (10)	14.600 ±.5164 (10)	0.138	15.000 ±0.000 (8)	15.000 ±0.000 (10)	-
2	SOFA**(≤2)**	1.900 ±1.7920 (10)	2.700 ±1.6364 (10)	0.311	0.625* ±1.4079 (8)	3.000 ±2.1602 (4)	0.111
3	APACHE II**(≤8)**	4.100 ±3.4785 (10)	3.8 ±2.3476 (10)	0.824	3.375 ±3.1595 (8)	3.500 ±1.7607 (6)	0.927
4	Marshall **(≤2)**	0.300 ±0.4830 (10)	1.600 ±0.9661 (10)	**0.002**	0.125 ±0.3536 (8)	1.833 ±1.1690 (6)	**0.015**
5	SIRS **(≤2)**	2.300 ±1.0593 (10)	2.600 ±0.6992 (10)	0.466	2.000 ±1.0690 (8)	2.000 ±0.8165 (10)	1.000

Values given are mean ± SD of the number of observations on day 1 and day 7 of treatment Values given in the parenthesis are the number of observations / subjects p value gives the statistical significance of the difference in the values for the given parameter in that group.* p< 0.02 by Student's't' test in control group: day 1 vs 7

Table2. *Some laboratory parameters in MSAP and SAP patients given control treatment alone or with parenteral Ala-Gln, on day 1and day 7 of administration*

S No	Parameter	Control Day 1	Parenteral Day 1	P value	Control Day7	Parenteral Day7	P value
1	BUN	20.320 ±11.5138(10)	35.100 ±18.9411 (10)	0.052	9.750* ±2.3441(6)	31.100 ±23.6194(10)	**0.019**
2	Creatinine	1.044 ±0.2603 (9)	0.830 ±0.2058 (10)	0.066	0.833 ±0.1033(6)	0.740 ±0.1776 (10)	0.205
3	SGOT	40.000 ±17.7764 (3)	45.100 ±26.3373 (10)	0.715	45.000 ±40.5339(5)	31.125 ±11.0639(8)	0.493
4	SGPT	25.000 ±3.6056 (3)	34.300 ±17.4677 (10)	0.144	31.400 ±15.8997(5)	30.125 ±23.9609(8)	0.910
5	ALP	142.000 ±168.5912(3)	105.500 ±61.8425 (10)	0.746	141.600 ±152.4247(5)	88.375 ±34.7643(8)	0.483

Values given are mean ± SD of the number of observations on day 1 and day 7 of treatment. Values given in the parenthesis are the number of observations / subjects p value gives the statistical significance of the difference in the values for the given parameter in that group.* p< 0.001 by Student's't' test in control group day 1 vs 7

Table3. *Comparison of the effects of enteral vs parenteral Ala – Gln administration on Disease Severity Scores in MSAP and SAP patients*

S No	Parameter	Enteral D7-D1	Parenteral D7-D1	P Value by "t"test
1	Glasgow COMA**(15)**	0.08±0.29 (12)	0.40±0.52 (10)	0.107
2	SOFA**(≤2)**	-1.07±1.21(14)	-0.75±1.70 (4)	0.743
3	APACHE II**(≤8)**	-3.14±2.60(14)	-1.17±2.23 (6)	0.112
4	Marshall **(≤2)**	-0.62±0.87 (13)	-0.17±1.33 (6)	0.474
5	SIRS **(≤2)**	-0.79±0.90(14)	-0.60±1.35 (10)	0.710

Values given are the mean ± SD of the differences in that parameter between day 7 and day 1 Values given in the parentheses are the pairs of observations / subjects p values given are for the differences in the effects on that parameter between the enteral and parenteral Ala- Gln groups by Student's t test

Table4. *Comparison of the effects of enteral vs parenteral Ala – Gln administration on some laboratory parameters in MSAP and SAP patients*

S No	Parameter	Enteral D7-D1	Parenteral D7-D1	P Value by "t"test
1	BUN	-1.13±7.08 (14)	-4.00±18.97 (10)	0.607
2	SGPT	-22.00±0.00 (2)	-0.25±10.30 (8)	**0.001***
3	ALP	2.50±9.20 (2)	-27.75±38.15 (8)	0.079

Values given are the mean ± SD of the differences in that parameter between day 7 and day 1Values given in the parentheses are the pairs of observations / subjects p values given are for the differences in the effects on that parameter between the enteral and parenteral Ala- Gln groups by Student's t test

Table5. *Effects of enteral and parenteral administration of Ala – Gln on total ICU stay and total hospital stay in MSAP and SAP patients*

S no	Group	Total ICU stay(no of days)	P value ANOVA	Total hospital stay(no of days)	P value ANOVA
1	Control	7.91±11.71 (22)	0.383	15.64±18.75 (22)	0.997
2	Enteral	8.31±5.80 (16)		15.59±10.27 (17)	
3	Parenteral	13.20±12.52 (10)		15.22±6.36 (9)	

Values given are mean ± SD of the number of observations / subjects given in parenthesis

RESULTS AND DISCUSSION

The study aimed to compare the beneficial effects of Ala – Gln administered enterally and parenterally to SAP and MSAP patients receiving standard enteral nutrition therapy. There fore to compare the study patients before treatment began, we determined the disease severity scores, liver and renal function parameters on day 1, before starting the treatment. These parameters, were determined again on day 7 of treatment, in addition to recording the total duration of stay of the patients in the hospital in general and that in the ICU inparticular.

It is evident from the results presented in tables 1and 2that onday 1 of treatment, patients in the control and parenteral AGD groups were in general comparable in the disease severity scores and in liver and kidney function parameters. In addition they were also comparable in several other parameters like vitals, haematological, pancreatic function (data not given). Although some parameters (e.g., BUN and Marshall score) were different between the groups, they were close either to the lowest or the highest value of the control range. Thus it appears overall that on day 1 of treatment, AP patients in the two groups of treatment could be considered comparable in general.

Elevated BUN is correlated with increased mortality in acute necrotizing pancreatitis and is predictive for ICU stay for survival [26]. Also, in critically ill patients with creatinine around 0.8–1.3 mg/dl, an elevated BUN is associated with increased mortality, independent of serum creatinine [27]. Thus increased BUN and unaltered serum creatinine seen in the AP patients of the two groups, appear to be in line with the above findings.

It is also evident from tables 1 and 2 that the significant differences observed between the two groups in Marshall Score and BUN, on day 1 of treatment, were observed even on day 7 of treatment, while the differences between the two groups in the other parameters tested, continued to be not significant at this time point. Although not significantly different, the disease severity scores appeared to be higher in parenteral AGD patients than controls, while the differences between the two groups in the LFT and RFT parameters were neither consistent nor significant on day 7 of treatment. These observations which were surprising, seem to suggest that parenteral AGD may not be associated much further benefits than control therapy *per se* in the MSAP and SAP patients.

Though not statistically significant, it was interesting that pancreatic necrosis and vital parameters (systolic BP, diastolic BP and respiratory rate) were lower in parenteral AGD group (data not given) than controls, perhaps suggesting its somewhat better benefits than control therapy. Indeed these observations in AP patients on parenteral AGD are in partial agreement with similar reports [28,29], that parenteral AGD in SAP patients had several beneficial effects such as, decreased disease severity, incidence of disease complications, hospital stay, length of ICU stay and mortality. However, itwas intriguing that SOFA, APACHE

and Marshall Scores were higher in parenteral AGD than control group, while Glasgow COMA and SIRS scores were comparable. Taken together, these results suggest that despite showing some improvement in a few associated parameters, parenteral AGD failed to influence disease severity probably due to insufficient magnitude of the effect on the associated parameters. It appears from comparing different parameters on day 7 of treatment that, over all, parenteral AGD may not be associated with significantly better benefits than control therapy *per se* in MSAP and SAP patients.

To assess if this was true or not, we tested in the two groups, day 7 values of different parameters with those on day 1 within the group. It is apparent from tables 1 and 2 that, 7 days of control therapy influenced only BUN and SOFA scoreand a few other parameters likeHb, HCT, plasma globulin (data not given), while parenterally administered AGD affected only body temperature (data not given) but not the disease severity scores. This inference appears to be in line with that drawn above, by comparing the values of different parameters between the two groups on day 7 of treatment.

An important objective of the present study was to compare enteral and parenteral routes of AGD administration and determine which would be the better one, vis a vis, the benefits in SAP and MSAP patients. Coincidentally, our group at the AIG,Hyderabad has very recently demonstrated that early, enteral (naso-jejunal tube) administration of AGD to MSAP and SAP patients was associated with better benefits than those seen with control / standard therapy *per se*.[30]To compare the effects of parenteral and enteral AGD, as also to assess which route of AGD administration was better in improving different parameters, we computed in both parenteral (present study) and enteral AGD administered patients [30],the difference($\pm$d) in the value of each parameter for each subject between day 7 and day 1of treatment and calculated the mean and SD of these differences for all subjects in that group. We then compared these mean $\pm$SD of the difference in the parenteral AGD group with that of the enteral AGD group, by Student's t test.

Results presented in tables 3 indicate that, although not significantly different, the magnitude of decrease in the disease severity scores was greater in enteral than parenteral AGD patients, probably suggesting that enteral AGD may have better benefits than parenteral AGD, in the MSAP and SAP patients. Among the associated parameters, the two groups differed in liver function tests (e.g., SGPT) (table 4) and vital parameters (data not given). However, the direction of change and magnitude of response in most of the associated parameters (day7 - day1 value), whether significant between groups or not, appeared to be favourable and better in enteral than parenteral AGD patients. It thus appears that the lack of significant differences between enteral and parenteral AGD, in the change in disease severity scores could be due to the insufficiency of the effects of enteral and parenteral AGDs on the associated parameters. Interestingly, these observations are similar to the ones we made in the enteral and parenteral groups while comparing the values of different parameters on day 7 with those on day 1 of the treatment. Considering that sample size was lower in both these groups, it may not be prudent to make any conclusive inference. Nevertheless, enteral AGD appears to be associated with better benefits than the parenteral AGD.

Indeed our observations and inferences drawn on enteral versus parenteral AGD administration are in agreement with similar reports in literature: Kalfarentzoset al [31], reported that enteral feeding was well tolerated, without adverse effects on the course of the disease, was associated with fewer total complications than those receiving parenteral nutrition and further, the cost of nutritional support was three times higher with parenteral nutrition. However, our findings are at variance with reports of i) Windsor et al [24] that glutamine supplementation through either route, reduced disease severity and improved clinical outcome and physiological parameters in AP patients given AGD enterally or parenterallyand ii).Zhao et al [23] that inflammatory markers decreased faster and to a greater extent in parenteral Glngroups compared to controls receiving TPN without Gln,and also decrease in disease severity scores (APACHE II and basal Balthaar's severity index).

It is intriguing that enteral rather than parenteral AGD had better benefits in the AP patients. Considering that i) enterocyte (GI tract) function is severely affected in AP and Gln is known to modulate gut permeability and ii) Gln, an important energy source to enterocytes, is depleted in hyper catabolic states such as AP and severe infections of the GI tract, our

observation of better benefits of enteral Gln (where Gln is directly delivered to the enterocytes) rather than parenteral Gln appears rational and reasonable. Indeed, Madhulika et al [30], have reported the favourable effects of enteral Gln on gastrointestinal absorption and alleviating the significant rise in the exocrine function of the pancreas.

Since enteral rather than parenteral AGD administration was associated with better benefits in SAP and MSAP patients, it was considered pertinent to assess whether they had any effect ontotal duration of the patients' stay in the hospital in general and that in ICU in particular. Notwithstanding the benefits associated with AGD administration, it was surprising the total duration of hospital stay was similar in all three groups: control, parenteral and enteral AGD (table 5). Also, it was equally intriguing that enteral AGD did not affect the duration of stay in ICU compared to that of controls. Though not statistically significant, it was interesting that duration of ICU stay was markedly higher in parenteral AGD patients (table 5). These findings disagree with those of Zhong, et al [32that parenteral Gln administration not only decreased the length of mean hospital stay in patients compared to controls but also that they experienced significantly shorter duration of nutrition therapy [33] and Stehle et al[29]that parenteral Gln dipeptide significantly reduced infectious complications, ICU and total hospital stay duration, mechanical ventilation duration and also lowered the hospital mortality rate but did not affect ICU mortality.However our observations agree with those of Sahin et al [34], who reported no differences in hospital stay ofAP patients receiving parenteral Gln compared to controls. Our failure to observe any effect of enteral or parenteral AGD administration on the duration of ICU or total hospital stay, could probably be due to the small sample size and / or the fact that the effect of enteral or parenteral AGD on various associated parameters and disease severity was insufficient to influence the hospital / ICU stay duration.

Notwithstanding that neither enteral nor parenteral AGD had statistically significant effects in MSAP and SAP patients, considering that i) parenteral AGDis more expensive than enteral (naso-jejunal) administration, which is easier and simpler than the parenteral route and ii) enteral AGD is better tolerated than gastric or duodenal supplementation, our findings though not statistically significant, suggest that enteralmay be better than the parenteral route for AGD administration to AP patients. They appear to warrant further studies in greater number of subjects not only to confirm these interesting findings but also to make early, enteral AGD administration mandatory in the treatment of MSAP and SAP patients.

SUMMARY

Moderately SAP (MSAP) / SAP patients were given standard therapy alone (group 1) or along with parenteral AGD (group 2). Effectsof treatment were assessed before (day 1) and after (day 7) treatment on several parameters (e.g., vital, haematological, liver, kidney and pancreatic functions, disease severity scores and duration of hospital and ICU stay. Many parameters were comparable between the two groups on day 1 of therapy. On day 7, BUN, serum creatinine, SOFA and Marshall Scores were indeed higher in parenteral AGD than control group. However in comparison with those on day 1, parenteral AGD showed significant change, only in body temperature and Glasgow COMA score on day 7, while standard treatment also affected Hb, HCT, plasma globulin, BUN and SOFA score. Although values on day 7 of treatment showed no significant differences between enteral and parenteral AGD patients, effects in enteral group were of greater magnitude and in right direction than those in parenteral group. Further, comparison of a parameter within the group, on day 7 versus 1 of treatment, indicated that enteral AGD was better than control and perhaps better than parenteral. Finally, testing differences in the value of a parameter (day 7-1) in enteral and parenteral groups, showed no significant differences between them in disease severity scores, although some parameters (liver function tests and vitals) showed significant differences. Nevertheless, the magnitude of change and its direction appeared to suggest enteral AGD to be better than parenteral. It was intriguing that neither enteral nor parenteral AGD had significant effect on total duration of hospital stay in general, or that in ICU in particular.

CONCLUSION

Notwithstanding that our finding:enteral rather than parenteral AGD has better benefits in SAP and MSAP patients is preliminary in nature, considering literature that enteral AGD which is at least as effective as parenteral AGD, is

simpler, feasible, less expensive and well tolerated in AP patients, we conclude with caution that, early enteral (naso-jejunal) administration of AGD to AP patients may be more beneficial than parenteral AGD. Nevertheless, the present leads warrant extensive studies in greater number of subjects, not only to confirm this finding but also to ensure that early enteral AGD is made mandatory in the therapy of AP.

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