Chapter 5

DISCUSSION AND SUMMARY

Discussion

Many of previous studies regarding the effects of megestrol acetate on body weight showed a consistence of increasing body weight in patients with various malignancies[2,59-61] and AIDS[65,66]. All of those studies were difference in dose and duration of evaluation. The usual minimum dose used was 160 mg/d in those studies. The present study tried to evaluate the lower dose of megestrol acetate compared to the conventional dose. Side effects of the treatment at low and conventional dose were negligible. Only one patient had a minor episode of vaginal bleeding. There was no difference in survival in both studied groups. The overall responses in term of weight gain in both arms were disappointed. Patients failed to gain weight in both studied groups after 4 weeks of MA. There were some possible explanations for failure. First, this study used lower dose and shorter duration of megestrol acetate comparing to other study. When comparing to the same dose and duration of study, there was one study that showed the similar percent of cases with actual weight gain (28%)[64]. Second, present study included patients with more severe weight loss (>10% from baseline). Third, the number of accrued patients was less than other major trials that showed the positive impacts of megestrol acetate. However, there were other interesting points to be discussed.

When considering the number of patients that had actual weight gain, there were more significant number of patients improving their weight in the conventional dose arm than the low dose arm, 36% versus 21%, respectively. To improve the power of detection in small sample size study, the 95% confident interval of means were shown to be compared. These results suggested a trend of positive dose response of megestrol acetate and body weight. It is interesting to note that even the low dose, 40 mg/d, MA

had a positive effect on body weight in certain number of patients as well. More samples may be needed to improve the power of detection and may show a clearer favorable outcome of the conventional dose megestrol acetate compared to the lower dose.

Interestingly, when considering the appetite stimulating effect, patients in both groups had appetite score improvement regardless of dose and overall weight change. There was slightly better score improvement in conventional dose arm but did not reach statistical significance. Possibly megestrol acetate might have a positive influence on patient's appetite even with low dose. While the net result of weight gain would require more than only the effect of appetite enhancement, such as metabolic change that favors fat deposition. Some studies showed that megestrol acetate promoted fat accumulation more than muscle mass[65]. This effect on fat metabolism might require a certain high enough dose of megestrol acetate.

The quality of life assessment also showed a similar trend of change. The patients in 160 mg/d MA group improved their total quality of life score after 4 week more than the 40 mg/d MA group. When considering the different aspects of assessment, there were the better scores in physical, family, emotional, and working status in the conventional dose arm. While the doctor relationship score showed no significant change. Although these data tended to favor the higher dose arm, there was no statistical difference in all of these aspects between both arms. The objective evaluation on performance status by investigator also confirmed the better trend of improvement in the conventional dose arm. From the subjective and objective evaluation, quality of life self assessment and performance status evaluation, megestrol acetate at higher dose showed a slightly better outcome in term of quality of life. However, the 40 mg/d MA cost is one third of the 160 mg/d MA at present. The justification of dose selection should concern not only the effect on weight but also the impact on other patient's concerns such as appetite enhancement, quality of life, and expense for the drug.

Data on anthropometric measurements were correlated with body weight change in this study. Both groups revealed decreased mid-arm circumference after 4 weeks duration. Tricep skinfold, which is though to represent body fat mass, was slightly improved in low dose group but not statistically significant. The anthropometric data confirmed that the major body compositions changed in cancer anorexia-cachexia are protein and fat loss. Although there was a discrepancy of data about fat and muscle loss among the studied groups, these may reflect an inaccuracy of anthropometric measurements which represented the indirect body composition assessment.

In the present study, the patients who also received chemotherapy or radiation significantly showed to have less weight gain. These may due to the majority of patients studied were cases of non small-cell lung cancer who should receive cisplatin based chemotherapy. It is widely known that cisplatin is one of the most emetogenic chemotherapeutic drugs. This may exert significant influence on patient's appetite. Moreover, regarding the quality of life assessment, score of emotional aspect supported previous explanation by showing a significantly lower score in the concurrent treatment arm than the other. Most of prior studies allowed certain accompanying therapy to the patients. Although there was no any study issued this potential problem, this potential impact should be considered in future study.

Conclusion

There were trends of better results with conventional dose of megestrol acetate in term of weight gain, quality of life score, appetite stimulation and performance status improvement although these did not reach statistical significance. Low dose megestrol acetate could increase appetite and slightly improve body weight of some cases with cancer anorexia-cachexia. Side effects of the treatment were negligible. Thus, conventional dose of megestrol acetate should be the more appropriate starting dose than the low dose megestrol acetate in the palliation of cancer anorexia-cachexia. From indirect assessment by anthropometric measurement, the present study confirmed that the major body compositions changed in cancer cachexia are fat and protein loss. Concomitant treatment had a significant influence on patient's weight gain and quality of life. Future study should aware this potential confounding effect of concurrent treatment of cancer.