

Quality of Life and Myelomeningocele: An Ethical and Evidence-Based Analysis of the Groningen Protocol

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Key Words

Myelomeningocele · Spina bifida · Neonatal euthanasia · Groningen protocol · Quality of life · Bioethics

Abstract

In 2005, a group of pediatricians at the University Medical Center in Groningen, The Netherlands, published the Groningen Protocol (GP) for Euthanasia in Newborns. This protocol is a set of guidelines devised in 2001 to clarify and facilitate the assessment of clinically stable neonates deemed to be in unbearable suffering for whom the prognosis is felt to be hopeless. At the time of publication, the GP had been in use for 7 years, and 22 patients, all with diagnosed myelomeningocele (MMC), had met the selection criteria for euthanasia by lethal injection. MMC is the most common neurological congenital anomaly, affecting approximately 300,000 newborns yearly worldwide. Neurosurgeons have a unique perspective on this disease and therefore an important voice, given the significant role they have in caring for these patients at all stages of their lives. This paper reviews the principal ethical arguments presented to date in the literature regarding the GP. It also provides an evidence-based critique of the GP in light of quality-of-life studies addressing adults with MMC, and ascertains whether or not the GP meets the criteria for an evidence-based guideline.

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Background/Introduction

In 2005, a group of pediatricians at the University Medical Center in Groningen, The Netherlands, published the Groningen Protocol (GP) for Euthanasia in Newborns in the *New England Journal of Medicine*. The protocol is a set of guidelines devised in 2001, according to the authors, to clarify and facilitate the assessment of clinically stable neonates deemed to be in unbearable suffering for whom the prognosis is felt to be hopeless [1]. Although known to take place and debated openly for decades, euthanasia was not officially regulated in The Netherlands until 2002 as a means to address end-of-life requests in exceptional cases of extreme suffering in competent adult patients [2]. As defined by Dutch law, euthanasia is death resulting from medication that is administered by a doctor with the explicit intention of hastening death at the explicit request of the patient [3]. Therefore, by this definition, actively ending the life of a neonate is not euthanasia and is illegal. Hence, the protocol additionally provides a measure of safeguard from prosecution for attending physicians who actively end the lives of neonates. At the time of publication, the GP had been in use for 7 years, and 22 patients, all with diagnosed myelomeningocele (MMC), had met the selection criteria for euthanasia by lethal injection [1]. This publication was understandably controversial and received a great deal of

attention in the lay press at the time. There was also a significant degree of condemnation, as well as support, from medical ethicists the world over. Interestingly, however, the neurosurgical community has remained largely mute on the subject. One exception to this silence is Dr. Rob de Jong, a pediatric neurosurgeon from Rotterdam, The Netherlands, who has been vocal in his opposition to the GP [4]. Neurosurgeons have a unique perspective on this condition and therefore an important voice, given the significant role they have in caring for patients with spina bifida at all stages of their lives. As opposed to neonatologists, who generally have a brief but intense clinical relationship with MMC newborns, both pediatric and adult neurosurgeons manage the various manifestations and sequelae of this condition into childhood, adolescence and adulthood. This paper presents a review of the principal ethical arguments presented to date in the literature regarding the GP. It also provides an evidence-based critique of the GP in light of quality-of-life studies addressing adults with MMC, and ascertains whether or not the GP meets the criteria for an evidence-based guideline (EBG).

The authors of the GP have been criticized for choosing to use the term 'neonatal euthanasia', yet for clarity, and in the absence of an alternative and universally accepted term, it will be used for the purpose of this manuscript.

The GP Summarized

The GP was created to address a small and difficult-to-define population of patients born with severe, albeit nonterminal, congenital anomalies. The considerations used to support the decision to end the lives of these children are fivefold. The first is extreme and sustained suffering and poor quality of life in terms of functional disability, pain, discomfort, poor prognosis and hopelessness. The second consideration is a predicted lack of self-sufficiency. The third consideration is a predicted inability to communicate and the fourth is expected hospital dependency. The final consideration is an expectation of prolonged survival [1].

In addition to the abovementioned considerations, five requirements must be fulfilled in order to carry out the decision to end the patient's life. Firstly, the diagnosis and prognosis must be certain. Secondly, hopeless and unbearable suffering must be present. Thirdly, the first and second requirements must be confirmed by at least one physician not involved in the patient's care. Addition-

ally, both parents must give informed consent. Lastly, the procedure ending the patient's life itself must be performed in accordance with the accepted medical standard [1]. Ultimately, the GP applies to a small and select group of infants with a 'hopeless prognosis' whom 'parents and medical experts deem to be in unbearable suffering'.

'Although it is difficult to define in the abstract, this group includes patients who are not dependent on intensive medical treatment but for whom a very poor quality of life, associated with sustained suffering, is predicted. For example, a child with the most serious form of spina bifida will have an extremely poor quality of life, even after many operations' [1].

Although in theory, the protocol is applicable to any condition meeting the abovementioned considerations and requirements, all patients to whom it has been applied were diagnosed with MMC.

MMC: Our Evolving Understanding

MMC is the most common neurological congenital anomaly, affecting approximately 300,000 newborns yearly worldwide. The incidence, approximately 1 per 1,000 in the USA, varies widely among different populations and ethnicities [5]. The incidence rate has declined significantly in the developed world since periconceptual folic acid supplementation for women of childbearing age has become standard of care. The impetus for this public health revolution was a multicenter, double-blinded, placebo-controlled study conducted by the UK Medical Research Council. The findings of the study were a remarkable 72% risk reduction in infants born with neural tube defects to women who took folic acid 6 weeks prior to conception [6]. Another significant contributor to incidence reduction is the increased sensitivity and widespread use of prenatal diagnostic tests such as serum α -fetoprotein, amniocentesis and ultrasound, and the subsequent implications of a diagnosis of MMC. An Australian study reported an 84% decrease in infants born with spina bifida between 1986 and 1991, attributable to prenatal detection and subsequent iatrogenic abortion [7]. A more recent publication from the UK followed 74 cases of prenatally diagnosed spina bifida. Termination of pregnancy was elected in 72% of the cases [8].

Clearly, the incidence of newborns with spina bifida has been reduced dramatically in the past two decades, but what is the current prognosis for the cohort of patients that come to term? The infant/early childhood

mortality rate quoted is in the order of 15% [9]. As this figure refers to a study in which patients were treated in a nonselective manner, it may be inferred that those who died suffered from the most severe forms of the disease manifested by hindbrain malformation, for which heroic measures either failed or were ultimately withheld. Recent long-term quality-of-life and survival studies in patients also treated nonselectively, which remains standard of care in North America, suggest that those patients who survive childhood fare better than has been historically believed [9, 10].

Additionally, there has been a resurgence in interest in surgical intervention in utero for fetuses diagnosed with MMC. In utero surgery is technically feasible and has been performed at several centers for more than a decade. The recent attention is in part due to study results suggesting a therapeutic benefit of fetal surgery with a reduction of hindbrain herniation and shunt dependence without an increase in either fetal mortality or maternal morbidity [11, 12]. Presupposing that the neurodevelopmental deficits common to patients with MMC are in part acquired, fetal surgery holds much promise as an emerging therapeutic alternative. These exciting new developments raise novel ethical issues in themselves however, principally in addressing the rights of the fetus as patient. The absolute benefits of in utero MMC closure are as yet unproven, and a randomized prospective multicenter trial is currently underway (MOMS trial) [13].

The Protocol: An Ethical Analysis

Is there a subset of patients born with spina bifida who are better off dead? Most would agree that not every life must be saved and that the answer to that difficult question is yes. However, how that death is attained is of critical importance to many. The practice of euthanasia is one of the most contentious topics in medical ethics. Jurisdictions exist where euthanasia is accepted by the medical and legal establishments and widely practiced, including Belgium and The Netherlands. Euthanasia is permitted in competent adults based primarily on the fundamental tenet of principlism, that is the respect for patient autonomy. However, even using the term 'euthanasia' is problematic in the context of neonates as they cannot be considered autonomous persons. This ambiguity of terminology has generated debate in and of itself. Other language for actively ending the life of a newborn has been proposed ('ending life') to avoid this confusion, but so far no alternatives have been universally adopted [14].

In order to debate the specific merits of the GP, certain assumptions must be entertained. The first is the ethical grounds for euthanasia in principle at all. As pointed out by Kon [15], inherent in a debate on nonvoluntary euthanasia is the assumed permissibility of voluntary euthanasia. While this remains a volatile and active debate, this article presumes euthanasia in competent adults is morally permissible for argument's sake.

The fundamental ethical justification by the authors of the GP for neonatal euthanasia of stable infants with a hopeless prognosis is the principle of beneficence. Ending the lives of infants who are suffering is justifiable if it is believed there are no other therapeutic alternatives [16]. Proponents argue that continuing life actually constitutes harm, and therefore is in violation of the principle of nonmaleficence. If a humane death, even a nonvoluntary one, releases a patient from excruciating pain and suffering, then it cannot be considered harm [17].

Others see parental autonomy as the dominant applicable ethical principle. Although admittedly a difficult matter, subjective judgments with respect to quality of life and life expectancy are routinely made by physicians based on clinical criteria, and defenders of the GP argue that this particular context is no different [14]. In the case of the pediatric patient, we must defer to the autonomy of the family unit and allow parents to make informed choices they feel are in the best interest of their child [15].

Still others see this protocol and the practice of neonatal euthanasia as appropriate in the unique context of contemporary Dutch culture [14]. This claim is supported by the fact that both the Dutch Medical Association and the Dutch Pediatric Association have issued separate reports legitimating the practices prescribed in the GP [18].

Those critical of the GP argue that nonvoluntary euthanasia 'violates ... the moral charge to do no harm' and in fact is not only morally unacceptable, but is a breach of traditional physician ethical codes of conduct, as well as an affront to the values of 'the overwhelming majority of the citizens of the world' [19]. Others are critical of parental roles in decision-making [20].

These critics and others also have concerns with the terminology and vagueness of the protocol itself, or what Chervenak et al. [20] called its 'clinical and ethical imprecision'. Making value judgments with respect to another human's quality of life (i.e. 'the hopeless and unbearable condition') is problematic. Is there any human condition completely devoid of hope? How does one determine what is unbearable to another? The only way of knowing is via the communication of a competent and autono-

mous person. This is obviously not the case in neonates devoid of a sense of self. Infants can experience extreme pain but they cannot suffer, anymore than they can hope for improvement in their condition.

Perhaps the most compelling ethical argument against neonatal euthanasia is that it is an injustice not to provide care to this cohort of babies based on a physician's decision as to what is acceptable current and future quality of life in what are, at best, uncertain situations [19]. It has even been suggested that the practices drawn up in the GP are a violation of numerous articles of the United Nations Universal Declaration of Human Rights, such as those including the right to life, as well as the rights of nondiscrimination and the right to equal protection by the law [4].

And thus, the seemingly competing tenets of principlism – respect for autonomy, beneficence, nonmaleficence and justice – serve to form the core arguments both for and against the practice of neonatal euthanasia. Although principlism is an important and influential model, which has to a significant degree permeated and dominated modern bioethical clinical discourse, we propose an alternative approach to critically reflect on the practices drawn up in the GP. Through a critical analysis of recent publications evaluating the long-term quality of life of patients with MMC treated in a nonselective manner, we may conclude whether or not the GP may be ethically applied to this cohort of patients.

The Protocol: An Evidence-Based Analysis

The GP must be analyzed both in the manner in which it was written and in the context it has been applied. In all of the 22 instances of reported termination of life of newborns between 1997 and 2004, the diagnosis of 'severe spina bifida' was made [21]. While all five considerations constituting the framework for which patients are selected for inclusion are surrogate markers for both present and future quality of life, we focus on the first two. The first consideration makes it explicit.

'Extremely Poor Quality of Life (Suffering) in Terms of Functional Disability, Pain, Discomfort, Poor Prognosis, and Hopelessness'

Each case reviewed by Verhagen et al. [21] was deemed to meet the criteria for extreme and hopeless suffering, pain and discomfort. Although the exact definition of 'hopeless and unbearable suffering' is unspecified, we infer it to mean acute and chronic pain that is not alleviated

by modern therapeutics. In fact, whether infants with open MMC actually experience an unbearable degree of pain is itself a matter of debate [4, 15]. The evidence is sparse, and no rigorous studies evaluating patients using the many available neonatal and infant pain scales have been published. Why adequate analgesia could not be delivered to this group of patients has been questioned as well [4]. A literature review by this author, as well as others, could not reveal any studies addressing pain in neonates with MMC, and one must conclude that it is not a dominant feature of the condition [4]. The Rotterdam Prospective Study on Discomfort in MMC currently being conducted will hopefully shed light on this specific matter [4].

'Predicted Lack of Self-Sufficiency'

With respect to the second criterion, in the absence of a clear definition by the authors, we take this to refer to the domains of ambulation, self-care and bladder control. This criterion was also judged to be met in all 22 cases reviewed.

The assumption of the authors of the GP is that the expected survival of this cohort would result in children, adolescents and young adults with an unacceptably low quality of life. Although there were limited data available on quality of life in adult patients with MMC at the time the GP was published, there have been important studies published in the interim. In fact, there is now literature supporting the notion that young adults with MMC have measured quality-of-life scores ranking very closely to nonaffected controls [10]. The fact that medical professionals and caregivers, including family members, overestimate the burden of disease and underestimate quality of life has been well validated in a wide variety of disabilities. There are often major discrepancies in perception between doctors and patients, particularly in subjective domains [22].

Quality of life assessments and data should be integrated into clinical decision-making when available. The largest study to date concerning life satisfaction in 119 patients with MMC and hydrocephalus concluded that there was nearly equal overall quality of life as compared to an age-matched peer cohort. As may be expected, patients with MMC were less satisfied with both their sex lives and self-care ability than the general population. Interestingly, however, these patients had greater satisfaction in the domains of finance and family life than the control group. Overall, 24% of the patients with MMC and associated hydrocephalus were dissatisfied with their lives, in comparison to 28% of the population

reference group. Another important finding of this study was that the severity of disease and the level of the lesion had little bearing on self-reported quality of life, and the authors concluded that spina bifida 'does not seem to be an important determinant of life satisfaction' [10].

There is little doubt that in this era of prenatal screening, with rates of pregnancy termination for diagnosed cases approaching 80%, the prognosis for those born with MMC has improved since the most severely affected fetuses are much less likely to come to term. Prenatal selection as well as improved perinatal medical and surgical care have improved neurological outcome [8]. Recent published reports with long-term outcomes at several decades reveal that the clinical outcome for patients with MMC treated in a nonselective manner is extremely variable, ranging from severe cognitive and motor disability to near normal neurological status. Hunt and Oakeshott [23] reported retrospectively on a cohort of 117 patients born with open MMC who had achieved an average of 35 years of age. Fifty-four percent of the patients had died. Of the survivors, over 40% lived and managed transportation, continence care and all other medical needs independently. Other outcome studies in those patients who survive infancy reveal that many patients are faring much better than this. In a 25-year follow-up of 118 patients born with MMC and treated in a nonselective manner, Bowman et al. [9] reported that 75% of the patients reached their early adult years; 85% of these survivors either attend or have graduated from high school or college, 80% of the patients are able to maintain social bladder continence via clean intermittent catheterization, and nearly 90% of the patients report acceptable levels of bowel continence. With respect to morbidity, 86% of long-term survivors are shunt dependent. In fact, the most significant cause of death in childhood or early adulthood was an unrecognized shunt malfunction. Although MMC is without a doubt a condition with significant mortality and morbidity, recent evidence suggests that with aggressive modern management, clinical outcomes may not be as dismal as historically believed.

Based on the arguments outlined above, we agree with Chervenak et al. [24], who conclude that the GP is scientifically invalid. The premise on which it guides clinical decisions is not supported by current evidence, nor by evidence available to the authors in 2004. Moreover, the authors do not include any sources or references supporting the assertion that patients living with MMC do so in unbearable suffering, with a poor quality of life and with-

out the ability to communicate. There is mounting evidence that many patients with MMC will lead relatively long and satisfied lives. There is no doubt that many will consume a disproportionate amount of medical resources and undergo numerous admissions and operations. Such is the case for many conditions, in both pediatric and adult medicine. These final two factors can hardly be viewed as evidence supporting the practice of nonvoluntary euthanasia.

Discussion

Evidence-based medicine (EBM) aims to provide the best available care to patients based on informed clinical decisions supported by scientific research. By EBM one assesses and ranks the quality of evidence and the risks and benefits pertaining to a particular treatment or lack thereof. 'EBM is a set of principles and methods intended to ensure that to the greatest extent possible, medical decisions, guidelines, and other types of policies are based on and consistent with good evidence of effectiveness and benefit' [25]. Two types of EBM have been described, EBG and evidence-based individual decision-making. EBG refers to developing official policies and protocols for groups of patients, not on subjective opinions or consensus, but on the best evidence available. It is now widely accepted that the adoption of organizational or institutional guidelines should be, when at all possible, based on an evidence-based approach. Evidence-based individual decision-making refers the judicious use of the best available evidence when an individual physician treats an individual patient [25].

With the spread of EBM there has developed a parallel 'evidence-based ethics' in order to integrate ethics into clinical decision-making [26]. This does not suggest, however, that there is a linear relationship between evidence and ethics, or that ethical decisions must always be evidence based. In fact, evidence comes in many forms and at various levels of quality. In the present situation, however, where future quality of life is the central matter at stake, available evidence can be a robust way to support an ethical stance. Clinicians and ethicists have a moral imperative to clarify the given situation as much as possible, to provide 'lucidity' [27]. Failure to do so may lessen the quality of decisions made and ultimately harm the patient. According to this analysis the GP, as it has been applied, is incongruous with current available evidence and fails to meet the definition of an EBG.

Conclusion

Nonselective treatment for newborns with MMC is currently standard of care in most of the Western world and should continue to be so. Each patient's case is unique, however, and an appreciation of when medical intervention becomes futile is paramount.

There is no reason to doubt that the patients for whom the GP has been applied were severely affected, nor is it the case that every means should be employed to keep all patients alive. Nor is there reason to believe that the physicians who drew up the protocol and were involved in the implementation of it did so for any other reason than out of compassion for these unfortunate infants. Whatever the intentions of those involved, however, active nonvoluntary euthanasia in neonates born with MMC must be condemned as unethical. This author agrees with Jotkowitz et al. [19] that deciding that any nonterminally ill

patients have 'no prospect for a future' is a dangerous precedent to set and one that has broad moral implications. Ultimately, what the supporting literature we have based our argument on implies is that we cannot always accurately predict the future. MMC in and of itself is not a terminal illness when treated actively and it is becoming evident that the majority of these patients, even those severely affected, will survive to develop into dignified adults who are satisfied with their lives [10].

The purpose of the discipline of bioethics is to set limits, but bioethicists require the expertise of clinical specialists to inform their limiting decisions. Formal neurosurgical involvement in ethical discussions of these kinds is vital. The criteria outlined for patient selection in the GP are not supported by long-term quality-of-life evidence pertaining to patients with MMC. The neurosurgical community is urged to reject it unconditionally.

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